# consultant



October 1961

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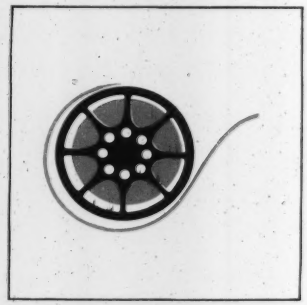

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October 1961



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# CORRESPONDENCE

CONSULTANT welcomes questions and comments about any of the topics covered. The authors will answer all questions by mail, and some of the most informative replies will be published in this section (names will be withheld on request). Please address all correspondence to CONSULTANT, SK&F Laboratories, 1500 Spring Garden Street, Philadelphia 1, Pa.

## Dramatic Success With Cardiac Massage in Drowning

(Consultant, August '61)

*Sir:*

*When I returned from my vacation I found your correspondence of August 1961 particularly interesting as to the first letter on "cardiac massage and drowning." This is how I handled such a situation on July 22, 1961. I was in my beach apartment at Ocean Gate, N. J. in full dress–a pair of swimming trunks. A woman yelled in: "Doctor, please come quick. A baby has drowned. He is not breathing." I followed her into the ground floor apartment of the next house. A 35 lb. two-year-old boy had been dragged out of the water by his six-year-old sister. His 235 lb. father, a Bell Telephone Co. executive who had been taught first aid, attempted to clear the boy's throat, looked into the child's mouth, saw the water level in his pharynx and decided that mouth-to-mouth resuscitation was not feasible. He placed him face down on a firm couch and instituted forceful Shaeffer (prone pressure) resuscitation–without effect. A nurse came in to help and sent the woman for me.*

*The child was cold, grayish white, pulseless, not breathing–apparently dead. His abdomen was markedly distended. Water bubbled from his nose and mouth. I suspended him by the heels with my right hand, rested his shoulders against the edge of the couch, placed the heel of my left hand over the lower sternum–in order to combine cardiac massage with artificial respiration–and jackknifed the boy rhythmically while depressing the sternum. Jets of water showered the spectators. I never have heard a more welcome sound than his first cough and cry. Incidental measures included maintaining airway manually with the help of a teaspoon; and blankets and elevation of buttocks while waiting for an ambulance. 1500 cc. of fluid were removed by nasal gastric tube at the Paul Kimball Hospital in Lakewood, N. J., while the boy was observed for brain, lung or other complications. He made a perfect recovery.*

– Henry A. Arkless, M.D.
Philadelphia

## Psoriasis and Arthritis

(Consultant, August '61)

*Dear Doctor Farber:*

*How often does arthritis occur in connection with psoriasis?*

– E. J. Wylie, M.D.
Watertown, Massachusetts

The incidence of arthritis in patients with psoriasis varies somewhat with the author. O'Leary reported a 15% incidence, which is in close agreement with the figure of 14% given by Lobitz and Brunsting on 500 cases. These two figures probably are high since they represent patient material of The Mayo Clinic where quite severe psoriasis is seen. Lower figures are probably more correct.

Pillsbury has reported a 1% incidence and we personally have noted a 3% incidence in a pilot study of over 300 patients.

– Joseph B. Peterson, M.D.

## Infantile Eczema?

*Sir:*

*It is reported that infantile eczema is most usually seen after two months of age. I have seen quite a number of eczematoid lesions occurring much earlier than this. Many times, but not always, changing from cow's milk will improve the condition. The strange part about it is, on many occasions the infant may not be seen again for six to eight months. On questioning the mother she will say, "I went back to cow's milk in two, three or four months and there was no recurrence of the condition."*

– Henry C. Petersen, M.D.
Stockton, California

Rashes in early infancy are common, and the rash you describe is not usually considered due to milk allergy.

At about one month of age, infants may develop a greasy scalp with a seborrheic rash starting on the forehead and behind the ears, later spreading to the cheeks. This is characteristic of Leiner's disease (seborrheic dermatitis) and is self-limited, usually requiring no treatment. It disappears at 3-6 months of age. For severe cases, washing with a mild soap frequently helps. This is well described in pediatric texts.

Another rash, however, which is not well described, appears as erythematous pimples at 4-8 weeks in almost all children. This has been attributed to milk, orange juice, or cereal sensitivity. It is probably not due to any of these, as almost all children get this rash, irrespective of diet. The rash usually lasts only two to four weeks. No treatment is necessary.

– Lewis A. Barness, M.D.

## Pregnancy in Double Cervix and Uterus

*Sir:*

*I have a 24-year-old, unmarried, para 0, gravida 1 female, now about five months pregnant, who has a double cervix and uterus (presumably) and a vaginal septum. The fetus is definitely lying on the left side of the abdomen. I would assume the left uterus is carrying the pregnancy.*

*What do you recommend? A trial of labor, and then if labor is prolonged, section? Do you recommend removal of the septum now? If not now, then sometime postpartum? What is the danger of the septum tearing during labor and third-stage hemorrhage?*

– Charles J. Kurth, M.D.
Sierra Madre, California

Your letter with the questions concerning the 24-year-old, five months pregnant girl with a double cervix and uterus and a vaginal septum was referred to me for reply. In general my philosophy underlying treatment of duplications of the human reproductive canal is to do nothing unless it is required. One must remember that dogs, cats, rabbits, guinea pigs and others have complete duplication of the reproductive apparatus and that they get along perfectly well without any difficulties from this duplicate uterus. It is rare for there to be such a total duplication in the human as you have encountered.

I would anticipate a perfectly normal first stage of labor with cervical dilation and with normal descent of the head. It is entirely possible that the septum may divide and reduce vaginal size sufficiently to interfere with the vaginal passage of the head. In that event all you have to do is incise the septum with scissors at the time of labor. Optionally you could excise the septum now. If it isn't done now and if you don't have to do it at the time of labor then I wouldn't do anything to the woman. Rather than a tear of the septum during labor such a septum as this generally prevents the passage of the head, and thus produces dystocia. If you incise the septum during labor it will probably be desirable to expose the vagina after the baby is born and to insure that there is no small bleeding artery. I would be most happy to have you drop me a note after the event and tell me how it all came out.

– William F. Mengert, M.D.

## Desensitization to Insect Antigens

(Consultant, August '61)

*Dear Doctor Feinberg:*

*You assume that the patient "needs protection from all the major species of stinging insects." If you can detect specific venom allergy by scratch-test techniques, why not simply desensitize the patient to the single insect species? Then, the patient's lack of information as to exactly which insect stung him becomes of lesser importance.*

– Seymour S. Cutler, M.D.
Brooklyn, New York

Antigenic relationships follow pretty much the lines of generic relationships. Thus, while there is generic relationship between the horse and the zebra, the fox and the dog, the melon and the cucumber, the mustard and the cabbage, timothy and corn, there are also differences between these related forms. The same applies to antigens (allergens) producing allergy. There are antigens which are common for mustard and cabbage and there are those specific for cabbage. Depending on which the person is allergic to determines whether he is allergic to one or both. Because it is not usually possible to determine this difference, we have found it advisable to include in the elimination or desensitization program the actual species to which the person is exposed. In the case of bees it is not always possible to determine which species was responsible for the sting–hence all the common species are included.

– Samuel M. Feinberg, M.D.

## P.S. About Vasectomy

(Consultant, August '61)

*Sir:*

*You may wish to publish the following in view of the great interest shown in fatherhood after resection of the vas–bilateral, of course. A husband in the above circumstance–double vasectomy some years earlier–and a pregnant wife appealed to the surgeon for an opinion. Was it possible for him to be the expectant father? The doctor sat behind his desk, chin in hand. The pregnant woman stood behind her husband. She shook her head violently up and down. The doctor spoke. "Yes, but not twice."*

*So endeth the lesson. I heard this story well nigh half a century ago from my preceptor the late Walter Brooks Brouner, M.D.*

– Herman Goodman, M.D.
New York City

# SURGERY

**L. Kraeer Ferguson, M.D.**
**University of Pennsylvania**

*L. Kraeer Ferguson, Chairman of the Department of Surgery of the Graduate School of the University of Pennsylvania, presents the concluding article in his series on office treatment of anal lesions. In the September issue of CONSULTANT, he discussed the diagnosis of a variety of common anal lesions and the treatment of fissures, external hemorrhoids, and hypertrophic papillae. Now he turns his attention to treatment of anal infections.*

# OFFICE TREATMENT OF ANAL INFECTIONS

If I could redesign the human body, one of my major changes would be to eliminate *anal crypts*. How admirably efficient and trouble-free the anorectal area would be without them; they are the main source of infection of the anal canal. But, unfortunately, crypts are with us to stay, because they are produced by the action of the sphincter muscle, a structure of overriding importance in preserving man's dignity.

The contraction of the sphincter puckers the mucosa above the mucocutaneous junction to form columnar folds and, at their distal end, the cup-like, infection-prone crypts. Because of their location, they are subject to injury by firm stools being squeezed into the narrowing anal canal. They are threatened by the hard stools of constipation, by the frequent stools of colitis or ileitis, and by the frequent anal spasms of diarrhea. The deep recesses collect infectious material and prevent drainage when infection occurs. Buried in the mucosal lining of the crypts are tortuous glands, which do nothing so well as furnish a pathway for infection from the crypt to the lymphatic tissue adjoining the rectal canal.

### The Numerous Paths of Infection

Each of the lesions shown in Figure 1 is a consequence of *cryptitis*, the localized infection of the crypt mucosa, glands, and lymphoid tissue. The infection may spread from the original site by burrowing either caudally or laterally from the anal canal. If the infection burrows caudally between the mucous membrane and the sphincter muscles, it may form a *perianal abscess*. If the infection burrows laterally through the external sphincter

or between the external and internal sphincter muscles, it may enter the fatty tissue of the ischiorectal fossa and form an *ischiorectal abscess*. This abscess may become quite large, for nothing in the fatty tissue between the anal canal and the tuberosity of the ischium hinders the rapid spread of infection.

Finally, a *fistula-in-ano* may result when the infection forms a tubular tract lined with granulation tissue and extending from the infected crypt to the surface of the skin near the anal orifice. Healing of one fistula may give rise to branching tracts opening at other points on the perianal skin but all arising from the same crypt.

This description of the infectious process implies that the treatment must include the site of the original infection. *If cure is to be permanent, the infected crypt must be identified and adequately drained.* Sometimes overriding considerations may limit treatment to simple drainage of the abscess, but recurrence should always be anticipated.

**Cryptitis**

Cryptitis is asymptomatic until inflammation spreads to the papillae and adjacent anal skin at the mucocutaneous junction. The painful passing of a stool over the inflamed papillae causes spasm of the sphincter muscle. The continued pain after defecation is due to irritation of the inflamed papillae caught in the grip of this muscle spasm. These symptoms, pain and spasm aggravated by defecation, are similar to the symptoms of fissure-in-ano, which were described in my article last month. However, cryptitis is easily diagnosed by palpation of the anal canal as fol-

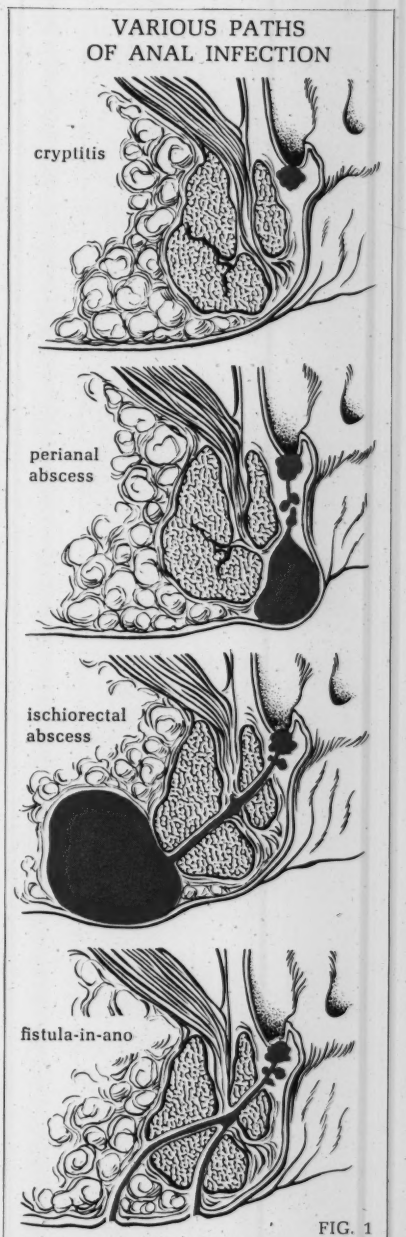


FIG. 1

lows. Because the infected crypt is usually situated posterior to the midline, you will cause less discomfort to the patient if you introduce your finger along the anterior anal wall. Then rotate your finger and gently feel the edematous papilla overlying the crypt. With a lighted anoscope, you can identify the infected crypt by hooking a probe into the deep, painful pocket.

Conservative treatment of cryptitis is worth a try. It consists of irrigation of the lower rectum with warm saline solution to reduce inflammation, sitz baths to relax the spasm of the sphincter muscles, and a bland diet with mineral oil added to soften the stools. If these measures fail, surgery should be performed as follows. Identify the infected crypt with a hooked probe, and infiltrate the overlying transitional epithelium of the anal canal with 1% Novocaine.® Then, using the hook as a tractor, cut away the overhanging tissue with scissors. A piece of Gelfoam® inserted into the anal canal will control the small amount of bleeding that may occur. Instruct the patient to take sitz baths after each bowel movement. With adequate drainage of the crypt, inflammation subsides within a short time.

**Perianal Abscess**

This abscess appears as a painful, reddened swelling at the posterior midline of the anal orifice. By spreading the buttocks, you can usually see pus expelled from the infected crypt by pressure applied to the abscess. Not only the abscess but also the infected anal crypt should be incised.

Under observation through an anoscope, locate the involved crypt by passing a hooked probe through the crypt and into the abscess. With 1% Novocaine,® infiltrate the overlying skin from the infected crypt to the farthest point of the abscess wall. Deep anesthesia is unnecessary; the patient will experience relief rather than pain when the abscess is incised and the pus is released. Extend the incision to the crypt, and cut away the edges of the skin to completely drain the whole area of infection. After gently removing all purulent material with a cotton sponge, pack the cavity with a small piece of gauze, and apply a Kotex-type dressing. The packing can be removed after three or four days; the wound will heal by granulation. Prescribe a normal diet in order to produce firm stools because they are less likely to infect the wound than soft or liquid stools.

**Ischiorectal Abscess**

The ischiorectal abscess can be easily recognized as a reddened, acutely tender area on one side or the other of the anus. Palpation of the rectal canal will reveal a hard, tender mass. It can be treated as an office procedure by incision and drainage of the abscess alone; this will relieve the pain, but the abscess is likely to recur because the infected anal crypt remains. Drainage of both the abscess and the crypt is usually performed in the operating room because spinal or deep general anesthetic is needed.

**Fistula-In-Ano**

The symptoms of fistula-in-ano are diagnostic. The patient will report drainage of a thick, malodorous material from the fistula onto his underclothes. Palpations of the rectal wall will reveal the hard, fibrous tract of the fistula, which will roll under the exploring finger.

If the tract is short, it may be excised

as an office procedure using a local anesthetic. Push a probe through the cutaneous opening and the tract to the anal opening. Then infiltrate the overlying tissue with 1% Novocaine® and, using the probe as a guide, lay open the entire length of the tract. An alternative method is to excise the fistulous tract if it has become fibrous enough to remain intact.

## *QUESTIONS AND ANSWERS*

**Q.** *Does fistula-in-ano sometimes heal spontaneously?*

**A.** Patients sometimes mistake the formation of scar over the cutaneous opening for permanent healing, but this is merely a stage in the infectious process. The dammed-up pus may form another fistulous tract or a blisterlike swelling behind the scar. The scar will either rupture spontaneously or have to be opened to relieve the pain.

**Q.** *How can irritation of the buttocks due to moisture from anal wounds be prevented?*

**A.** Maceration of the skin between the buttocks can be prevented by applying zinc oxide ointment. Also, the patient must wear a Kotex-type dressing until the wound heals completely.

# LARYNGOLOGY

**Albert P. Seltzer, M.D.**
**University of Pennsylvania**

*Albert P. Seltzer is Chief of the Ear, Nose and Throat Departments at Philadelphia General Hospital and Mercy-Douglass Hospital; senior attending physician at Albert Einstein Medical Center; and Associate Professor of Otolaryngology at the University of Pennsylvania Graduate School of Medicine. He is author of the text PLASTIC SURGERY OF THE NOSE (Lippincott) and other books and articles. In his third contribution to CONSULTANT, Dr. Seltzer reviews some common causes of foul breath and methods he has found effective in diagnosis and treatment.*

## FOUL BREATH AND ITS MANY CAUSES

Foul breath is not only the social handicap the ads tell about; it can be a clue to an infection, allergy, or some other disorder unsuspected by the patient and often no place near the mouth. It may, for example, be a clue to a liver disorder, when the odor resembles indol. Or to post-surgical complications, including fecal impaction, peritonitis, acute gastric dilatation, and lung abscess, when the odor resembles boiled cabbage.

Most often, however, the cause of foul breath will be found in the mouth or upper respiratory tract. Decaying teeth and unhealthy gums are common causes. And the teeth, natural or artificial, can be traps for food particles. But there is another food trap commonly overlooked—a cleft tongue. Careful investigation of the back of the tongue will sometimes uncover a transverse pocket containing fermenting food particles. Cleaning out the depressed space will remove the breath odor.

When simple hygienic measures are called for, I remind the patient about the need for carefully brushing the teeth and recommend rinsing the mouth with a solution of a teaspoonful of salt mixed in a glass of water. For patients who aren't sensitive to iodine, I suggest adding one or two drops to the solution.

Long-standing mouth breathing, due to nasal blockage, may cause offensive breath by drying out normal secretion and facilitating entrance

into the oral cavity by various microorganisms. Mouth breathing may result from swollen turbinates, an allergic condition, diseased adenoids, polyps, or some other growth. Odor in such cases can only be stopped by locating and correcting the pathologic condition.

**Nasopharyngeal Sources of Foul Breath**

In the nasopharynx, a chronic, low-grade pharyngitis leads to alteration of the cells of the lining membrane, with loss of normal ciliary action and a change in the nature of the secretions; unpleasant breath odor results. Infected tonsils may have a similar effect. Even though the tonsils may not appear to be enlarged, the crypts may be loaded with microorganisms. The tonsils should be probed or the mucosal lining swabbed to obtain a culture in order to identify the organisms and prescribe proper therapy.

Infection in the nasal cavity can cause foul breath. Any type of rhinitis can be the cause, but especially the atrophic form in which the normal mucosal function is largely destroyed, causing ozena. Cure of ozena usually requires building up the patient's over-all resistance by improved nutrition and proper rest, as well as outdoor exercise. Vitamin A and D supplements are often needed, and sometimes vitamin $B_{12}$ and iron. I have sometimes found that patients were helped by hydrocortisone or estrogens, though I try these measures only in refractory cases.

The most effective local treatment is nasal irrigation with saline solution once or twice a week, and I often instill Argyrol 5% solution. I try to limit these measures to office practice, for although patients can learn to inhale saline solution, they too often get both solution and exudate back into the eustachian tube, adding to their troubles. They should be warned against excessive use of Argyrol. As they do other good medications, they tend to overuse Argyrol, with harmful results that are well known . . . but not by laymen.

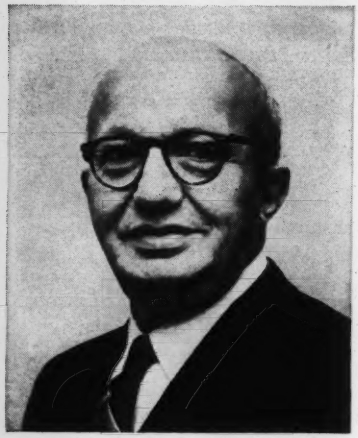
Any intranasal disorder in which there is necrosis or ulcer formation, particularly when there is bleeding with accumulation of blood anywhere along the upper respiratory tract, is apt to cause foul breath due to the breakdown of blood constituents. Postnasal drip, if long continued, is also likely to cause it.

Infected paranasal sinuses can cause breath odor, as can other respiratory tract infections. Chronic bronchitis, bronchiectasis, lung abscess, and gangrene can too, and lung infection by inhaled organisms of Vincent's angina. As with suspected infection of the pharynx, proper therapy of respiratory tract infections naturally depends upon identifying the offending organisms and determining their sensitivity to antibiotics or sulfa drugs.

**Determining the Cause**

To determine the cause of breath odor, a careful history is the first requisite, followed by a physical examination to rule out liver disease, intestinal and gastric disorders, and possible disorders of the upper respiratory region. Finding decayed teeth does not necessarily mean that referral to a dentist will solve the problem; the patient may also have sinusitis or other upper respiratory infection, or an intestinal disorder.

# LARYNGOLOGY



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**Locating the Source of Odor**

To determine whether the odor arises in the nose or mouth, have the patient close his lips firmly and exhale forcibly through his nostrils; this breath will come directly from the nasopharynx and nose without passing through the mouth. Then close the nostrils firmly by pinching with thumb and finger, ask the patient to hold his breath a moment and then allow air in the oral cavity to escape *without force*. This will test the odor of the mouth which can be compared with that from the lungs and bronchi by repeating the pinched-nose test, but with *forcible* exhalation through the mouth.

The patient cannot always be depended on to know when his breath is offensive, since long-standing odors may be unnoticed after he becomes accustomed to them. Also, the olfactory sense varies in acuteness in different individuals. Therefore, the physician must assume responsibility for telling patients about conditions that should be corrected . . . and for reassuring them when their fears are unwarranted.

## *QUESTIONS AND ANSWERS*

**Q.** *Do you find that many patients imagine they have bad breath?*

**A.** Yes, and with the constant bombardment of advertising on the subject, it is surprising there aren't more breath-odor hypochondriacs. If these patients can't accept reassurance, they should be referred for psychiatric help. Some patients who are obsessed with the belief that they have bad breath may actually create the condition by excessive rinsing and gargling with strong commercial mouthwashes. Overuse of some preparations can damage mucosal tissue and impair the flow of natural secretions.

**Q.** *Do you ever recommend mouthwashes?*

**A.** Not specifically, though if the patient uses one sensibly and likes it, I don't try to prevent it. I recommend a simple saline solution where it seems indicated. I do tell patients who use garlic heavily or some other seasoning that causes breath odor that they can mask it with 'Sen-Sen', chewing gum, candy mint, or something of that sort.

**Q.** *Is there anything patients with cleft tongue can do to clean out the food that collects?*

**A.** They can be taught to create a gag reflex by reaching back into the throat with a finger, while simultaneously coughing vigorously. This will empty the crypt and then they can rinse thoroughly with mild saline solution. Doing this once a day, morning or evening, will keep the area from collecting food particles.

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He's 'riding high' with 'Troph-Iron'!"

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*Smith Kline & French Laboratories, Philadelphia* SK&F

# PSYCHIATRY

**John L. Schimel, M.D.**
**New York City**

*John L. Schimel is a Fellow of the American Psychiatric Association and a Charter Fellow and Treasurer of the Academy of Psychoanalysis. He is a graduate cum laude of the Georgetown University School of Medicine. In addition to his private practice, Dr. Schimel is Director of Psychiatry at the Hebrew Home for the Aged of Riverdale, N. Y., a member of the faculty of the William Alanson White Institute of Psychiatry, and has recently completed a book for adolescents, HOW TO BE AN ADOLESCENT AND SURVIVE.*

## THE CHILD WHO WON'T GO TO SCHOOL

Most of us can recall the tricks we used and the plans we made to avoid a day at school—and not get caught. The child who *won't* go to school is another matter. The intense dread that appears in such children will not be eliminated by increasing discipline. I do not know of any statistics concerning the incidence of school phobias, but my experience suggests it is a fairly common occurrence and one the family physician is often asked to handle.

### Premonitory Signs

Such phobias do not develop "out of the blue." There are usually premonitory signs. The children I have treated had all been examined by a physician at least once before they were brought to me. Often they had been taken to their family doctor repeatedly for apparently trivial matters – the child usually complains of headache or abdominal pain. The physician's negative medical report often forces the phobia into the open for the first time.

In other children, unaccountably slow recovery following a serious illness was the warning sign. Faced with a child's vague complaints and unhappy appearance, the physician may initiate additional studies in an attempt to find some organic cause, and thus

delay the correct diagnosis. I believe you should consider the possibility of school phobia in every child with an unusually prolonged convalescence. Although the clinical picture varies, an unreasoning dread of returning to school is always present and if you talk to the child about the imminence of his return to school, it may become apparent.

### The Older Child

In the older child, this dread may not be apparent until the moment of return occurs. He may seem to listen to reason, agree to return to school, and may even profess to be somewhat enthusiastic – until the day arrives. At this, the critical moment in all cases, the underlying fear breaks through. Usually, it will be accompanied by non-specific somatic complaints, or complaints that may follow classical hysterical patterns. His behavior may deteriorate markedly and include prolonged crying, depression, and even a mention of suicide.

### The Parents

Naturally enough, the child's behavior during these episodes frightens and distresses his parents. As they become progressively more concerned about the child's behavior, they may become difficult to deal with. When they visit you, you may see marvelous demonstrations of ambivalence—expressions of both love and rage toward the child. Since you will usually become the target for some of this rage, you will be wise to remind yourself that this is a good time to keep your head.

### Thorough History Essential

As with all medical problems, a thorough history is essential to proper treatment. Ordinarily, you will learn that the child has been a diligent worker and has tried hard to get good grades and to please his parents and teachers. He will usually have been mannerly and congenial, and will continue to be so save during the outbursts of the phobia—characteristics which make his obduracy on these occasions even more shocking. The parents usually have set high standards for the child, and are ambitious for him. From these parents, more than others, you will hear, "I only want what is good for him." While this is a quite common parental feeling, in these families the children are overly concerned about their ability to meet the standards that have been set for them.

### The Schoolteacher

While it may be a novel experience, you should, whenever possible, discuss the child with his teacher. You may find that the information she (perhaps only she) can offer will be invaluable. Occasionally, a short conversation with the teacher will reveal that the cause of the child's fear is fairly simple; he may be afraid of a classmate, for example. Rarely, the teacher herself may be the immediate cause. I once saw what might be called an epidemic of school phobias that was triggered by an unsuitable substitute teacher.

### Problem Usually More Complex

Usually, however, while some acute problem may have triggered the outburst of the phobia, neither the cause nor the solution will be so simple. Ordinarily, you will find that you are dealing with a chronically anxious child who has always been very concerned about his performance, and

who had been growing increasingly more tense prior to the appearance of the phobia. The chronic tension may have been aggravated by discord in the home or some change in the school situation. In the adolescent, concern about physical changes accompanying puberty may be the source of aggravation.

### Phobia Is an Emergency

Regardless of the underlying psychological factors, the phobia constitutes an emergency and should be treated as such. If the situation is not handled promptly and effectively, the child's motivation may steadily erode as he gets further and further behind his group and begins to feel more and more hopeless. For the adolescent in particular, the phobia may mark the end of all effective schooling. A total push, including drugs if necessary, is indicated. Most important, however, is a firm, calm, and clear insistence on the necessity of a prompt return to school.

### Consult and Support Parents

Probably nothing will vitiate your efforts more effectively than parental differences of opinion about what should be done, and the child may play one against the other. Since these situations can easily destroy whatever unity of purpose and decision the parents ordinarily have, they will need support and guidance so that one does not undo the efforts of the other, and both should be involved in your planning of what is to be done.

I make a point of telling parents that they cannot expect quick and easy improvement. The child will probably continue to react to going back to school as he has in the past—crying, screaming, illness, etc.—and may even develop new symptoms. I make it clear that the parents must deal with these attempts firmly; that the father may have to drive the child to school because his behavior on the school bus is too disturbing; that they will have to control, subdue, or simply put up with the embarrassment the child's "scenes" may create. At the same time, though, some compromises are possible. While the child must go to school, he need not spend the entire day with his class. Perhaps he need stay only for the morning session or he may be introduced to the full routine even more gradually. One 11-year-old girl, for example, was permitted to spend much of her first week back at school in the visiting room of the assistant principal. For some children, particularly those who have fallen quite a bit behind in their work, tutoring can be a valuable adjunct to treatment. I stress, however, that such tutoring can only supplement, not substitute for, regular school attendance. A professional tutor is best and parents are least helpful in this role.

### Psychiatric Consultation

Finally, although few of these children are as psychiatrically ill as they seem to be during the critical phase of the phobia, psychiatric consultation is indicated since the school phobia may be a manifestation of an ominous psychiatric condition. In no case, however, should the procedures outlined above be delayed until such consultation can be arranged. Meticulous attention to historical factors, clarity and firmness with child and parents, and the use of all measures available to support and reassure the child, and get him back in school, may avert a serious condition.

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Prescribing information adopted January 1961.

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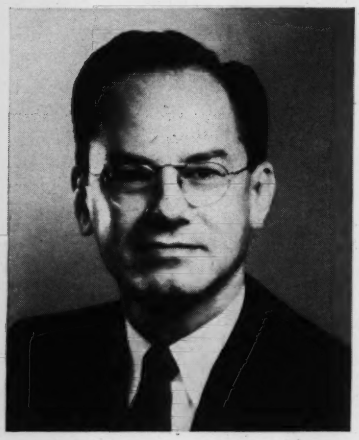
# GASTROENTEROLOGY



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## "STOMACH REST" IN THE EARLY MANAGEMENT OF PEPTIC ULCER

The majority of patients with peptic ulcer disease referred to me have failed to respond to treatment. What treatment failed? Usually I find it was something like the following:

— three bland meals a day

— a snack or glass of milk between meals

— antacid tablets before and after meals

— antispasmodics or anticholinergics and sedatives

This regimen is hazardous because it is just effective enough to encourage its routine use. On the average, 4 out of 5 patients will do well on it. But the remaining patient simply gets worse: his pain returns; his ulcer enlarges or penetrates. Eventually he may require surgery — surgery that with better treatment might have been avoided, or at least postponed long enough to permit a safe and definitive procedure to be performed.

In contrast, almost all patients will respond if a "stomach rest" regimen is followed. I recently had the occasion to review the case histories of 100 outpatients who had been referred for treatment of their ulcer. For weeks, months, or even years in some, they had been on a regimen similar to that outlined above. (One man with a penetrating ulcer had been hospitalized for six months in a psychiatric ward for "functional back pain".) But in all of them, in spite of the duration of their illness, a "stomach rest" regimen relieved daytime symptoms, usually by the end of 12 to 48 hours. For

those who had symptoms continuously for several months or even longer, it required four to six days. In the management of early uncomplicated peptic ulcer, one can expect "stomach rest" to relieve symptoms much more rapidly; about 12 hours is the rule.

### Stomach Rest

The principle of rest is one of the common denominators in all medical treatment. When the heart has been damaged by a coronary occlusion, we cannot stop it from contracting, but we can limit the burden imposed upon it by restricting the activity of the patient. The same can be done with the ulcerated stomach or duodenum.

To promote healing, especially in the early stages, the stomach should be kept in a state of relative rest. The regimen used to accomplish this state of rest is based on the classic studies of A. J. Carlson, who found the introduction of a feeding temporarily inhibits peristaltic activity. This phenomenon he called receptive relaxation. The most vigorous peristaltic contractions, of course, occur in the empty stomach (hunger), and the next most vigorous are encountered as the stomach attempts to empty its contents after a full meal. Hourly small feedings, however, will avoid these extremes of motor activity and will repeatedly bring about receptive relaxation, thus maintaining a state of relative "stomach rest". In the early management of active peptic ulcer, the objective of treatment should be to keep the stomach and duodenum in this state.

### The Regimen

For most ambulatory patients, the regimen is begun with the ever-available milk feeding, 5 ounces every hour on the hour during the waking hours. When convenient, a similar quantity of Cream of Wheat, creamed soup of a vegetable puree, jello, custard or pudding may be substituted for the milk. On the half hour, midway between feedings, peristalsis begins to return only to be inhibited again by the ingestion of liquid or powdered antacids. Initially, I prefer liquid antacids to the tablets, because they mix more readily with gastric content and are more efficient in their capacity to neutralize the hydrochloric acid. Needless to say, the use of tobacco, alcohol and caffeine beverages is forbidden.

During this phase of management, I give a mild sedative, and to further reduce motor activity, a tolerance dose of an anticholinergic. By a tolerance dose, I mean *all* the anticholinergic the patient can tolerate without experiencing undue side effects. There is no "standard dose" of an anticholinergic agent. The amount prescribed should be determined by titrating the dose for each patient individually. The dose should be maintained just below that level which will cause blurring of vision. Such a "stomach rest" regimen is employed for 10 to 14 days before permitting any additional food items. Then gradually over a period of two months or so, the diet is advanced with stepwise increments providing five small meals and eventually three meals of bland, low-residue food with milk feedings between meals.

I have treated doctors, lawyers, mechanics, taxi cab drivers — all have carried their thermos of milk around with them, and they are glad to do it. After all, they have spent a great deal of time and money without getting

any results, and are only too happy to follow a regimen that works. So with patient cooperation presenting no problem, the majority of them can remain ambulatory. However, if they do not respond in a week's time, I hospitalize them. Getting them away from their home environment, business or other emotional strain is sometimes necessary before they respond to treatment.

Of course, when there is a confined perforation, the ulcer may heal temporarily only to break down as the diet is advanced in the second or third month. Surgery is frequently required in this group of patients. A period of preoperative "stomach rest" will usually permit the edema and inflammation to subside so that the surgery itself will be easier technically. Thus, the surgeon can perform a definitive procedure, such as a 50% resection with vagotomy or a 3/4 gastric resection. Otherwise, in the presence of a massive inflammatory reaction about a confined perforation, he may be forced to do a pyloric exclusion, or a gastroenterostomy and vagotomy. These compromise procedures are followed by a higher incidence of recurrent ulceration or gastric stasis.

**Stomach Acid: How Important?**

The dictum "no acid, no active peptic ulcer" has never been refuted, and there is no doubt that acid is essential to the pathogenesis of peptic ulceration. However, the level of free acid in the stomach remains relatively constant whether the ulcer is active or in remission. Thus, it would appear that a breakdown in mucosal resistance is an even more important factor in ulcer genesis. Furthermore, the relative importance of acid is revealed by the observation that even a "stomach rest" regimen, while it affords as effective a control of acid as possible, usually suppresses acid only slightly. I think we have deluded ourselves into thinking hourly feedings, hourly antacids and tolerance doses of anticholinergic can be depended upon to eliminate the acid factor. On the other hand, in spite of the relatively high level of acidity, the "stomach rest" regimen does facilitate ulcer healing. Many of the measures used to suppress secretion also depress motor activity. So, it would appear that avoiding mucosal irritants and putting the stomach and duodenum at motor rest are of greater importance in promoting ulcer healing than our ineffective, though desirable, efforts which only partially neutralize the acid.

Next month in CONSULTANT:

The Problem of Canker Sores – a practical review by Dr. E. William Rosenberg of Miami Medical School, discussing the "nuisance disease" that afflicts 1 out of every 5 people at some time in life.

Tonsils and Adenoids: When to Operate – some specific suggestions by Dr. Raymond S. Rosedale, a previous contributor to CONSULTANT.

# PEDIATRICS

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**Alan E. Holtzman, M.D.**
**U.C.L.A. Medical Center**

*Alan E. Holtzman is Assistant Clinical Professor of Pediatrics at UCLA and a member of the staff at several San Fernando Valley hospitals. His interest in the various phases of pediatric practice is reflected in his service on the Advisory Boards of the Children's Hospital Foundation, the Child Guidance Clinic and the Association for Gifted Children of San Fernando Valley. In addition to state and local societies, his professional affiliations include the American Academy of Pediatrics.*

# EPIGLOTTITIS: A FORGOTTEN DIAGNOSIS

Why the diagnosis of epiglottitis is so often missed is a puzzle. It is a fairly common disorder which has been recognized since 1905; it is always potentially dangerous, and sometimes rapidly fatal; and its signs and symptoms are plain to see. Yet, according to a recent report of 42 patients with epiglottitis, only one was referred to the hospital with the correct diagnosis. Perhaps the diagnosis is so often missed because the disorder comes on so abruptly and proceeds so rapidly from fever and sore throat to critical emergency.

We have seen twelve children with epiglottitis in the past two years, six of whom required tracheotomy as a life-saving measure. Here is one such case.

*A 6-year-old boy was hospitalized with acute upper respiratory obstruction. He had been well until the morning before admission when he complained of sore throat and lack of appetite; that afternoon, his physician noted mild pharyngitis and fever and prescribed tetracycline; by 8 o'clock the same evening, he had difficulty breathing and sat in bed drooling and having moderate inspiratory stridor. The alae nasae flared and suprasternal, intercostal, and lower sternal retractions were prominent. His epiglottis was severely inflamed and edematous, blocking inspiration.*

*At the hospital, he was treated with chloramphenicol, intramuscularly, and cold "steam" inhalations. After two hours there was no improvement in breathing, so tracheotomy was done. By the following morning, he was afebrile and had no respiratory distress. Chloramphenicol was continued by mouth and the tracheotomy tube was removed after 4 days. On the 5th day he was discharged. No significant organisms grew on cultures of the blood or on material from the throat, trachea and epiglottis.*

### Etiology

Acute epiglottitis is generally considered to be caused by *Hemophilus influenzae, Type B.* This organism has been the most common one cultured from the blood and from the throat of patients with this disease, although other organisms have been grown on cultures. Some investigators believe that epiglottitis is the secondary effect of some precursor disease, usually a viral infection, and is caused by organisms already present in the respiratory tract.

### Clinical Course

Epiglottitis usually affects children between two and six years of age and commonly occurs in the late fall, winter, and early spring. There have been scattered reports of its occurrence in both younger and older children, and in adults.

The disease is abrupt in onset, with fever and sore throat as prominent early symptoms: a younger child may merely gag while drinking. In the early stage, physical signs are unimpressive, the pharynx is only mildly hyperemic, and some of the anterior cervical lymph nodes slightly tender; dyspnea may or may not be present. So, whenever a child has soreness of the throat greater than seems consistent with its appearance, acute epiglottitis should be considered.

This early stage lasts only a few hours and is followed by what ought to be unmistakable symptoms—dyspnea, pallor, cyanosis, and prostration. Often, there is inspiratory stridor with pronounced suprasternal and infrasternal retraction. The patient sits up, leans forward, gasps for air with his mouth opened wide and tongue protruding, and drools excessively. Pulse and respiration rates are sharply accelerated and there is a muffled quality to the voice which is unlike the hoarseness seen with other laryngitides. The diagnosis can usually be confirmed just by looking at the epiglottis, which is easily exposed by depressing the tongue or by pulling the tongue forward. In most children, merely placing the blade on the tongue will cause the swollen, reddened epiglottis to rise into sight. Sometimes, however, in an older child, for example, the epiglottis can be seen only with the aid of a mirror.

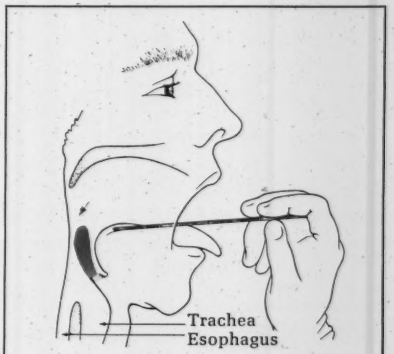


Figure 1. Note how the swollen epiglottis obstructs respiration and is visible when the tongue is depressed.

Inflammation and swelling are usually confined to the epiglottis, the aryepi-

glottis folds, and arytenoids. Some superficial ulceration of the mucosa may be present. Cultures of the blood or of material from the epiglottis and pharynx may grow *H. influenzae* or other organisms, as we said before.

**Differential Diagnosis**

Acute epiglottitis needs to be distinguished from spasmodic croup, acute laryngitis, and acute laryngotracheobronchitis. Spasmodic croup may or may not be preceded by mild upper respiratory symptoms. Typical barking cough is present and there may be slight fever; the epiglottis is not swollen or red as it is in epiglottitis. Spasmodic croup usually responds quickly to increasing the humidity of inspired air.

In acute laryngitis, involvement of the vocal cords is shown by definite hoarseness. There may be slight dyspnea at the onset. Aphonia suggests the possibility of diphtheric laryngitis.

Acute laryngotracheobronchitis is markedly slower in onset than acute epiglottitis. Usually, respiratory difficulty does not develop until after a day or two of illness; when it does develop, there is usually expiratory as well as inspiratory impairment, as against inspiratory only in epiglottitis. Rales may be heard in laryngotracheobronchitis, but are rare in epiglottitis.

**Treatment**

The primary consideration in managing the patient who has acute epiglottitis is early establishment of an adequate airway. If respiratory obstruction is not severe, increasing the humidity of inspired air may help to reduce the swelling of mucosal tissues; for this purpose, vaporized cold water appears to be superior to steam. Vaporizing apparatus consists of a nebulizer through which water can be forced by compressed air or oxygen. The nozzle should be placed close enough to the patient to permit large quantities of the cool vapor to reach the respiratory passages.

Chemotherapy should be started at once. Chloramphenicol should be given intramuscularly in dosages of 100 mg. per kg. of body weight per 24 hours for children up to 15 kg.; and 1 to 2 gm. per 24 hours for children over 15 kg. This daily dose should be given in three equal injections at 8-hour intervals. After the first day, chloramphenicol can be given orally at a dosage of 50 mg. per kg. of body weight per 24 hours.

*When the patient has pronounced suprasternal and intercostal in-drawing, or the pulse is increasing at the rate of ten per hour, or the respiratory rate is increasing, tracheotomy is mandatory.* Passing an endotracheal tube is not desirable because of the pre-existing inflammatory and edematous condition, except as a preliminary measure until a tracheotomy can be performed. Tracheotomy is preferably performed in the operating room under general anesthesia after an endotracheal tube is passed. Occasionally a temporary laryngeal obstruction may develop in the induction phase, but with the proper equipment at hand, the passage of an endotracheal tube is not a major problem.

Acute epiglottitis constitutes a real emergency and early recognition is vital. It is by no means a rare disease and we should keep it in mind as a possibility whenever we are asked to treat sore throat in children.

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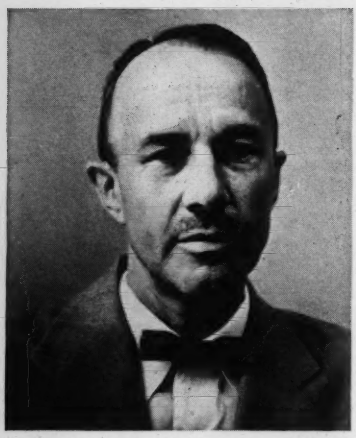
Prescribing information adopted January 1961.

# CARDIOLOGY



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# POINTERS FOR USING ANTICOAGULANTS

The techniques of administering anticoagulants have undergone, and are still undergoing, changes that should make them more useful than ever before in cardiovascular patients. Keeping up with the changes and trying to improve on them have occupied our interest over the years at Pennsylvania Hospital. The techniques we currently use are outlined in this article.

### Therapeutic Uses

Venous thrombosis, pulmonary embolism, increasing angina (or pre-infarction), and acute myocardial infarction are the main indications for anticoagulants. We usually begin therapy with heparin to provide a rapid effect. An initial dose of 50 to 100 mg. is given intravenously, followed in two or three hours by a subcutaneous dose of 100 to 140 mg. injected into deep subcutaneous tissue, over the lateral abdominal wall or in the flank. We use a 26 x ½ needle, taking care that the tip has no hook which can cause tissue damage and local hemorrhage.

Giving heparin subcutaneously (200 mg. or 20,000 units per cc. type) maintains its activity for 10 to 12 hours and overcomes the drawbacks of the older, less concentrated forms that had to be given more frequently. Identical doses are given twice daily, at 10 a.m., and 10 p.m. Peak drug activity usually occurs in about 4-6 hours.

The dose is regulated by the "clotting time", using the Lee-White method or

This article is based on a talk given by Dr. Vander Veer on "Radio Seminars," a weekly service provided by the Pennsylvania Hospital Continuation Education Program and supported in part by a grant-in-aid from SK&F Laboratories.

a modification of it. We usually do only one clotting time a day, at 9 a.m., before the morning dose. This clotting time should be about 12 or 15 minutes, or a little above the normal of 8 to 10 minutes. If, however, it is normal, the heparin dose is raised. If it is as high as 20 to 25 minutes, the next dose or even two doses should be lowered somewhat. If there is any question, the clotting test time should be repeated around 2 p.m., a convenient time for the personnel involved. Remember, though, drug action will be near its peak and, therefore, clotting time should be much higher than it was at 9 a.m. Clotting time for the afternoon test should be at least 20 to 25 minutes. If it is still low, a larger dose is needed. Occasionally a dose as large as 200 mg., twice daily, may be necessary.

In the first few days of therapy, we believe heparin alone is preferable to combined anticoagulants: it provides complete anticoagulant action within a few hours and, in our experience, it is easier and *safer* to control in the early, acute period of the illness. However, after subcutaneous heparin is continued for a week to 10 days, then one of the orally active anticoagulants is added to the regimen. Unlike heparin, the oral anticoagulants take from 1 to 3 days before they produce any significant effect, and probably from 1 to 2 weeks before a full therapeutic effect is obtained.

To regulate dosage of oral anticoagulants, daily one-stage prothrombin time tests are started. Normal prothrombin time is from 12 to 15 seconds. In the first few days of oral therapy, the time should be brought to around 25 to 35 seconds, that is, between 15 and 25 percent of normal. We do a test daily until prothrombin time is fairly well stabilized, usually around the 4th or 5th day of therapy. Heparin dosage then is gradually reduced over the next 5 or 6 days and then stopped completely. Tests of clotting time may usually be stopped during this "tapering off" period. When the prothrombin time is stabilized, it may be checked every other day, but it is seldom wise to do the test less frequently than every third day during the first few weeks of therapy.

In *increasing angina*, or what we like to call pre-infarction angina (impending infarction), the diagnosis must often be made from the clinical picture, since ECG tracings may be normal. Generally, if pain is relieved quickly by nitroglycerin, it is safe to start anticoagulant therapy, as described, along with other appropriate measures. Anticoagulant therapy is not without danger and requires that we be as certain as possible of the diagnosis before using it. It is vitally important to rule out conditions that mimic acute myocardial infarction, e.g., *dissecting aneurysm* and *upper abdominal emergencies*, where such therapy is bound to do harm.

#### Major Prophylactic Uses

Oral anticoagulant therapy usually begins in the hospital and continues for some time afterward. When patients are discharged, we do prothrombin tests on them weekly for the first few weeks to regulate dosage and maintain prothrombin time around 25 to 35 percent of normal, that is, at a level slightly higher than when the patients were hospitalized. Later we may run tests every two weeks, but a two-week interval is the longest we like to go. Intervals of

three or four weeks between tests often lead to difficulties, even in patients who seem to be easily regulated.

Prophylactic anticoagulant therapy is of real value in preventing further emboli in those with *peripheral* or *pulmonary embolism*. This type of patient often has atrial fibrillation and mitral stenosis. Even a small embolus in such patients is an indication for anticoagulants. In *chronic recurrent* phlebitis, these drugs can terminate a smoldering condition.

Increasing evidence points up the value of anticoagulants in preventing *recurrent myocardial infarctions*. We are all familiar with what may happen in second and third attacks. Not only is the patient likely to have shock, arrhythmias, or failure, but his chances of cheating sudden death are considerably reduced. So, if we can prevent thrombosis or delay an acute myocardial infarct, we will be doing such patients a real service.

Anticoagulants are indicated in all patients with a second or third attack and should be continued after the acute episode. Other measures are also important, such as: low-fat diet, no smoking, weight reduction if obese, control of hypertension, and so on.

Anticoagulants are usually indicated in those with chronic, severe angina, even though it may not be increasing. These patients usually have extensive coronary artery disease and an acute coronary episode, even a small one, is likely to produce a massive infarct with the well known consequences. With anticoagulants, we may have a chance to prevent or postpone this from happening.

Occasionally, a patient recovering from his first infarct may be a candidate for long-term anticoagulant therapy. This is especially true in one who has a severe infarct followed by angina or some failure, or when hypertension or angina have existed before the first infarct.

Finally, there is a group of susceptible, younger patients, usually males, who have had a first infarct and who have a bad family history of cardiovascular disease, high cholesterol, lipid disturbance, etc., who probably will benefit from long-term prophylaxis with oral anticoagulants.

A question often asked is how long anticoagulant therapy should be continued in patients with a relatively acute process such as acute uncomplicated thrombophlebitis or even acute myocardial infarction? Our experience convinces us that the initial heparin therapy of acute venous thrombosis is best followed by at least 2 or 3 weeks of oral anticoagulant which is then "tapered off". If a *short* period of heparin therapy is utilized in such patients, some of the "cures" will be followed by recurrences, even though the heparin therapy was terminated gradually. In uncomplicated first attacks of acute myocardial infarctions, it is our practice to continue the oral anticoagulant therapy for about three months after the patient has become ambulatory. At the end of this period the decision is made about continuing or tapering off the therapy, based on the clinical picture. There is increasing statistical evidence to prove the highest incidence of recurrence is in the first year after the acute attack. Time may prove it wise to continue the anticoagulant for at least this period of time, even in the milder cases.

**Stopping Anticoagulant Action**

If patients receiving anticoagulants develop bleeding or require surgery, their clotting mechanisms can be restored to normal in several ways. Simply stopping heparin terminates its action within hours. Or protamine sulfate, given intravenously in doses of 50 mg., quickly counteracts heparin action and restores coagulation to normal. Finally, fresh blood transfusion should be used in cases of severe hemorrhage to terminate the action of heparin and to restore blood volume.

In case of oral anticoagulants, one or two 5.0 to 10.0 mg. doses of Vitamin $K_1$ (Mephyton) will usually restore prothrombin to near normal levels within 24 hours, provided that patients do not have a greatly elevated time (lowered %), or have not been given an overdose of the drug. Large doses of Vitamin $K_1$ should be avoided, if possible, since they may make the patient refractory to further anticoagulant therapy for several days. If whole blood and Vitamin $K_1$ are used concomitantly to restore prothrombin levels, there is a real danger of thromboembolic complications. This is a calculated risk that must be taken occasionally. Finally, we again should stress the "tapering off" of oral anticoagulants when stopping therapy. This process should be very gradual, over at least 3 to 4 weeks' time, with weekly prothrombin tests continued.

# PARNATE®

brand of tranylcypromine

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- faster onset of action than any previously available antidepressant with similar indirect action
- specific antidepressant effect—relieves such primary symptoms as dejected mood, inactivity and inability to concentrate
- a new monoamine oxidase inhibitor—unrelated chemically to the hydrazine antidepressants
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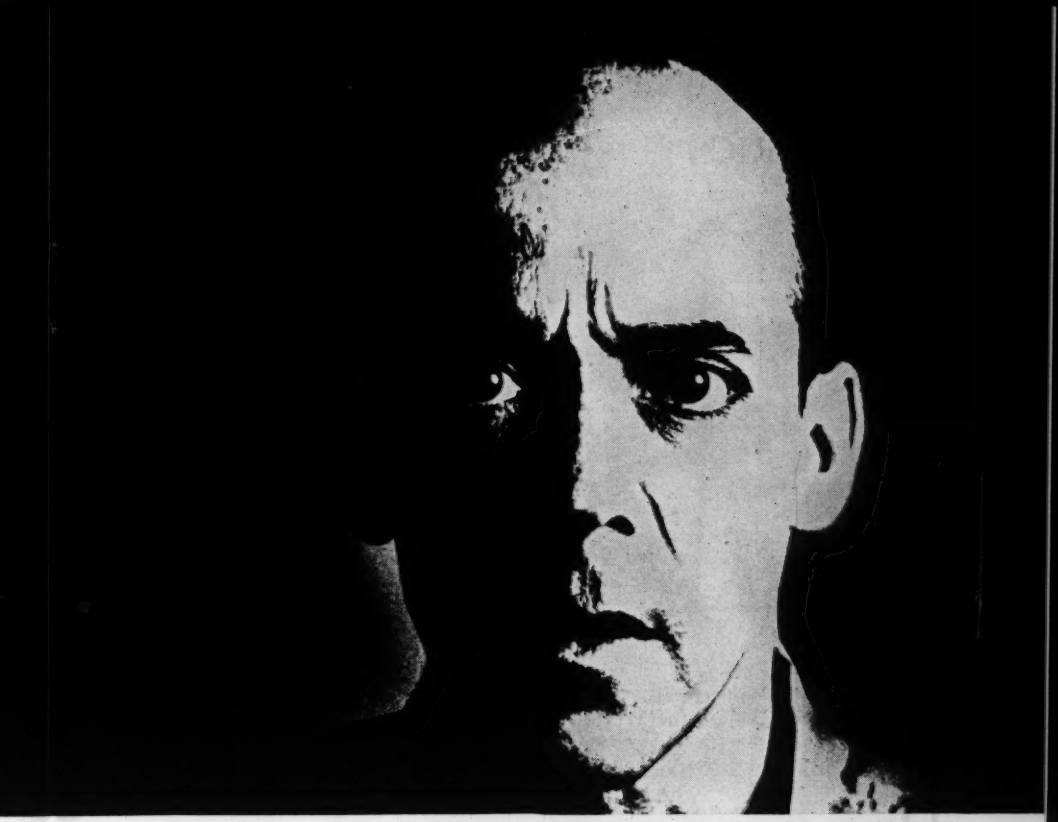
AVAILABLE: 'Parnate' Tablets, 10 mg., in bottles of 50. Each tablet contains 10 mg. of tranylcypromine (trans-*dl*-2-phenylcyclopropylamine) as the sulfate.

*For complete prescribing information, see back of magazine.*

SK&F leaders in psychopharmaceutical research



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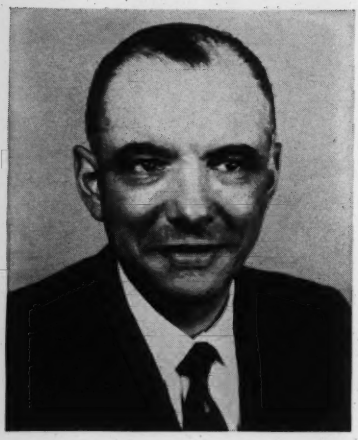
# OBSTETRICS



**Russell R. de Alvarez, M.D.**
**University of Washington**

*Russell R. de Alvarez is Professor of Obstetrics and Gynecology at the University of Washington School of Medicine and Obstetrician and Gynecologist at King County Hospital and University Hospital in Seattle. He is a graduate of the University of Michigan Medical School and the author of 70 papers on toxemia of pregnancy, fluid and electrolyte metabolism, and lipid and protein metabolism in pregnancy and neoplastic disease. He was formerly president of the Society for Gynecologic Investigation and Assistant Secretary of the American College of Obstetricians and Gynecologists.*

## HOW TO PREVENT ECLAMPSIA IN YOUR PRACTICE

In the state of Washington—and other areas of the country as well—preeclampsia-eclampsia is the foremost underlying cause of maternal death. It is also responsible for many fetal deaths, for when mothers die undelivered, babies die too. Even if the mother with eclampsia survives, her baby frequently does not.

Nobody knows what causes preeclampsia-eclampsia. Some change in renal hemodynamics results in the abnormal retention of sodium and water. As pregnancy advances, this positive water balance causes abnormal weight gain followed by rising blood pressure, proteinuria, and edema.

### Prenatal Care

The first signs of preeclampsia are subtle indeed. The patient will not notice them and neither will the physician unless he is especially alert for them. Therefore, I believe that prenatal visits should be scheduled for once every three weeks before the seventh month, once every two weeks during the seventh and eighth months, and once each week during the last month of pregnancy.

My own experience bears out the importance of prenatal care. At University Hospitals among our clinic patients, most of whom have had no prenatal care before admittance, the incidence of preeclampsia-eclampsia is about 12%. Under the most exacting prenatal care, the incidence is about 1½% of all obstetric patients. Furthermore, exacting prenatal care can reduce the incidence of eclampsia

among mothers with preeclampsia to less than ½ of 1%.

### Prophylaxis

Weight gain due to the pregnancy and its normal physiologic changes is about 15 pounds, and I try to limit my patients to that. Of course, this is not easy, but it is usually possible. I favor a daily diet for the normal pregnant patient of 2100 calories consisting of 100 grams of protein, 250 grams of carbohydrate, and the remainder of the calories made up of fats. Also, since changes in metabolism and renal function begin early in pregnancy, I believe that sodium intake should be restricted from the first prenatal visit until delivery. I instruct my patients to reduce their use of table salt and to avoid heavily salted foods throughout pregnancy. Incidentally, salt restriction need not mean an uninteresting diet, as Dr. Plotz points out in his article in this issue.

### First Signs of Preeclampsia

While prophylactic treatment can be expected to reduce the incidence of preeclampsia, the possibility that it may develop in any patient must always be foremost in our minds. The more quickly the subtle signs of early preeclampsia are recognized, the sooner vigorous treatment can begin. The earliest symptoms are likely to be a rising blood pressure and a sudden weight gain. Although prolonged gains of more than ½ pound weekly warn of possible trouble, sharp gains in weight in a short period of time (1½ to 2 pounds per week) are still more ominous. This is because gains in such a short period of time cannot be logically attributed to too many calories and hence are more likely to be caused by abnormal retention of water.

During normal pregnancy, the blood pressure does not rise; in fact, it usually falls and remains below normal until after delivery. Thus a rising pressure is never normal; when it occurs in the last trimester, it is usually a symptom of preeclampsia. It is unwise to define hypertension as blood pressure exceeding 140/90 mm. Hg., the accepted upper limit of normal in the non-pregnant patient. For instance, if your pregnant patient has a blood pressure of 90/60 in early pregnancy, an increase of 40/30 mm. could signal severe eclampsia, even though her blood pressure is not over 140/90. She is no less hypertensive than the patient whose blood pressure increased by the same amount from a "normal" of 120/80 to 160/110. Failure to recognize this fact probably explains the oft-described patient with convulsive eclampsia and a "normal" blood pressure.

### Other Early Signs

You do not have to be an ophthalmologist to recognize the early evidence of preeclampsia in the eye grounds. There is a slight swelling of the retinal walls, a slight attenuation of the retinal vessels, and the appearance of a shiny, glassy surface of the posterior retinal epithelium. These changes are depicted in Figure 1.

Proteinuria is usually a somewhat later development and hence is particularly serious. But remember one thing: Proteinuria in pregnant patients should be verified by testing a *catheterized* urine specimen. Voided specimens are apt to be contaminated, no matter how carefully collected. In consultation, I have seen several patients

who reportedly have "severe renal disease complicating pregnancy" only to find that the proteinuria was diagnosed from a voided specimen only, and that a catheterized specimen was completely free of protein.

Edema, so characteristic of eclampsia, is frequently not recognizable in mild preeclampsia. However, a tight-fitting ring or puffiness around the eyes will sometimes serve to confirm what earlier symptoms have already suggested.

Although not a clinical symptom, a previous history of toxemia in multigravidas is highly suggestive of recurrence.

* * *

To sum up, disciplined vigilance can prevent eclampsia. We must constantly remember how quickly normal pregnancy can become grossly abnormal, for the line between health and mild preeclampsia is thin. Similarly, when mild preeclampsia is evident, it should be regarded as the earliest phase of severe eclampsia because eclampsia can develop momentarily with grave implications for both mother and child.

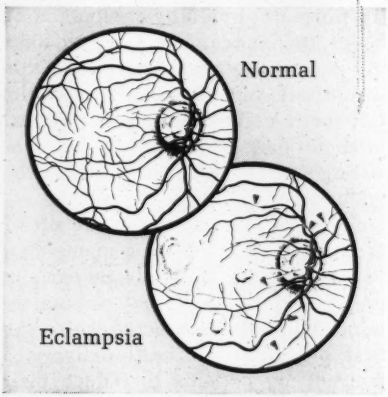



Fig. 1. Spasm of the arteries and seemingly fewer capillaries in the eye grounds is an early sign of preeclampsia. The sheen of edema is represented in the diagram by stippling.

## *QUESTIONS AND ANSWERS*

**Q.** *When should a patient be hospitalized for preeclampsia?*

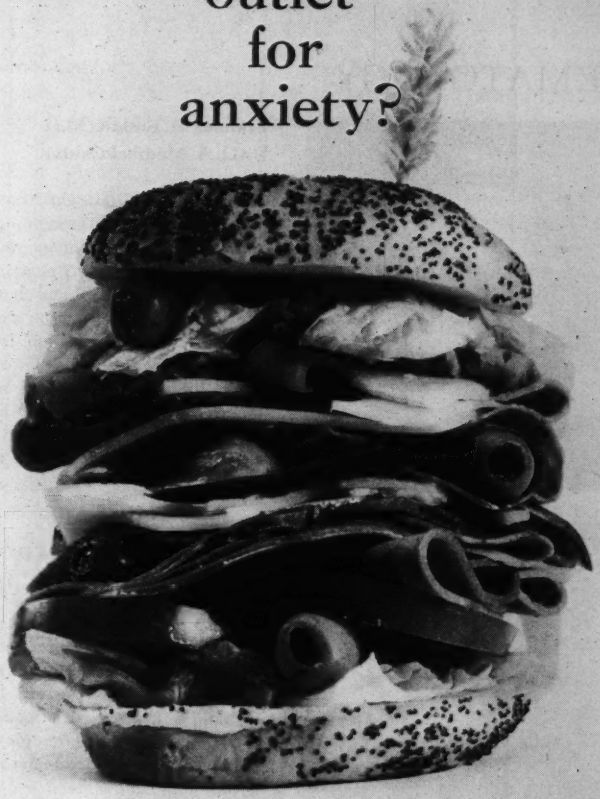
**A.** All but the mildest cases should be hospitalized. If the blood pressure has risen 40/30 mm. or more, if more than slight edema or proteinuria is noted, or if the patient is uncooperative or unintelligent, the risk of home treatment is too great, and the patient should be hospitalized.

**Q.** *What regimen do you recommend for home treatment of mild preeclampsia?*

**A.** Home treatment frequently fails unless the patient understands exactly what is expected of her. Often it is best if the first few days of treatment are under hospital supervision. I prescribe a diet of 1500 calories and 1 gm. sodium chloride, adequate fluid intake to insure urinary output of 2000 ml., 50 mg. of hydrochlorothiazide daily, and bed rest. The patient is examined every three days; if she does not improve, she is hospitalized for supervised treatment.

Further details about Dr. de Alvarez's treatment of mild preeclampsia may be obtained by writing to CONSULTANT, 1500 Spring Garden Street, Philadelphia 1, Pa.

# outlet for anxiety?



"Inasmuch as the act of eating has a tranquilizing effect, the chief psychologic function of overeating seems to be to reduce anxiety."

Kaplan, H.I., et al.: New York J. Med. *57*:2815.

In marked contrast to many anti-appetite drugs, 'Eskatrol' both controls appetite *and* relieves the psychic stress that causes overeating.

# ESKATROL® SPANSULE®

brand of sustained release capsules

**when the emotions play an important role in overweight**

Prescribing Information

FORMULA: Each 'Eskatrol' *Spansule* sustained release capsule contains Dexedrine® (brand of dextro amphetamine sulfate), 15 mg., and Compazine® (brand of prochlorperazine), 7.5 mg., as the dimaleate, distributed among hundreds of minute pellets with varying disintegration times. A therapeutic dose is released promptly and the remaining medication, released gradually and without interruption, sustains the effect for 10 to 12 hours.

INDICATION: 'Eskatrol' *Spansule* capsules are indicated in overweight patients, particularly in those who depend on eating for psychologic release.

'Eskatrol' *Spansule* capsules provide not only daylong control of appetite but also relief from the emotional stress associated with overeating and with dieting. The desire to eat is reduced and patients, particularly the so-called "compulsive eaters," feel better and are able to adjust to the weight-reducing program—*even for prolonged periods of time.*

RECOMMENDED DOSAGE: One 'Eskatrol' *Spansule* capsule daily, taken in the morning.

SIDE EFFECTS: Side effects (chiefly nervousness and insomnia) are infrequent, and usually mild and transitory.

CAUTIONS: Clinical experience has demonstrated that 'Eskatrol' (containing the phenothiazine derivative, 'Compazine') has a wide margin of safety and that there is little likelihood of blood or liver toxicity or neuromuscular reactions (extrapyramidal symptoms). The physician should be aware, however, of their possible occurrence.

'Eskatrol' *Spansule* capsules should be used with caution in the presence of severe hypertension, advanced cardiovascular disease, or extreme excitability.

AVAILABLE: In bottles of 30 and 250 capsules.

Prescribing information adopted Jan. 1961

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# DERMATOLOGY

**Frances M. Keddie, M.D.**
**U.C.L.A. Medical Center**

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**Thomas H. Sternberg, M.D.**
**U.C.L.A. Medical Center**

*Thomas H. Sternberg is an Assistant Dean and a Professor of Medicine (Dermatology) at the U.C.L.A. Medical Center. He received his medical education at Northwestern University Medical School in Chicago. He is a Diplomate of the American Board of Dermatology and Syphilology; Fellow, American Academy of Dermatology and Syphilology; and a member of the American Dermatologic Association. Dr. Sternberg has written many papers in dermatology and has co-authored and made contributions to several books in his specialty.*

## ACNE VULGARIS: CONCEPT AND CURRENT TREATMENT

Acne is an almost normal feature of adolescence, yet knowledge of its pathogenesis has accumulated slowly. From what we do know, it is fair to assume that the lesions of acne are associated with increased activity of hair follicles and sebaceous glands during adolescence. This increase seems to be touched off by a change in status of sex hormones. We know that acne is exceedingly rare during normal childhood and in people whose skin maintains the characteristics of childhood, either from hormonal lack or from inherited constitution. The texture of these skins can be considerably altered at any age by the administration of androgens, which will increase the growth of hair and sebaceous gland units and produce acne.

The degree of acne depends on the amount of hormones given and the susceptibility of the individual.

Hair and sebaceous glands, which form an inseparable unit on most parts of the skin, are the sites of acne lesions. Considering the dense population of these units on the face, it is remarkable that so few of them are affected. One fault leading to acne lesions is the closure of the gland orifice by keratin scales and sebum. In time, sebum and soft lanugo hairs pile up, rupture the follicle wall and spread into the dermis. As irritating foreign materials, they cause inflammation which, if it spreads to neighboring follicles, results in acne that is cystic, indurated, and scarring. Other faults, such as tissue edema and possible chemical alterations in sebum, require further study to determine their relationship to acne.

**Steroids**

In treating severe cystic and scarring acnes, which do so much damage to the psyche as well as to the skin, corticosteroids can be safely and successfully used to subdue the inflammation, no matter how severe. When steroids are given in sufficient doses for a long enough period of time, the response is rapid, and once inflammation has subsided, only small doses are necessary to sustain improvement. Failure frequently results when the initial dose is not large enough to cause prompt regression of the already existing lesions. Generally, we use, with good results, a starting daily dose of 16 to 24 mg. of triamcinolone or from 4 to 6 tablets of 0.75 mg. dexamethasone. This initial dosage is continued for one to two weeks. When improvement is satisfactory, a maintenance level is established by gradually decreasing the dose in the usual way. At first we used an antibiotic in conjunction with steroids but later found it unnecessary, except in rare instances. Ordinarily, complete control of this type of acne can be maintained with corticosteroids until such a time as the acne wears itself out and spontaneously disappears.

No conclusion can be drawn about the mode of action of the corticosteroids in acne. It may be that their success is due less to the suppression of the local inflammation than to some regulatory effect on the general hormonal situation. *We have not tried this treatment for juvenile or ordinary pustular acne nor do we advise it.* However, it does provide a method of preventing the severe scarring associated with deep cystic and pustular acne. And in our experience the prolonged use of corticosteroids in young people, with proper medical control, has not been accompanied by any serious side effects.

**Antibiotics**

Although antibiotics frequently control inflammation in acne, the reason they do is not entirely clear. The explanation that micro-organisms in the lesions contribute to the inflammation and are inhibited or destroyed by antibiotics may, in part, be true. However, acne lesions are frequently found to be sterile for bacteria. Furthermore, the doses that are effective are usually much lower than those needed to control systemic infections. For example, acne inflammation may be controlled with as little as 125-250 mg. of tetracycline daily.

**Topical Therapy**

In less severe cases the most widely used remedies are cleansing and de-

greasing agents to relieve the superficial plugs in the follicles. Used alone or with keratolytic agents they prevent, to some extent, the more serious and extensive pustular and cystic lesions from developing.

Today the best of these preparations are combinations of drying and keratolytic agents, with specially prepared sulfur, in a lotion or in a greaseless base. Many are tinted and so act to cover the lesions as well as to treat them. Additional topical therapy with lotions containing antibiotics and steroids are frequently useful to control superficial irritation and infection.

A final note on topical care: telling adolescents not to pick or squeeze lesions is well meant but seldom followed advice. Instead they can be told to use a hot compress and gentle pressure to remove excess sebum from some lesions and to use a drying lotion afterward.

#### Diet and Drugs

Almost all patients suspect that what they eat either causes or contributes to their acne. And generally most practitioners tell their acne patients to eliminate certain foods. Except for chocolate, shellfish, and halogen compounds, food and drugs seem to make little difference in the severity or duration of acne. Certainly the sebaceous glands manufacture the sebum, probably from the glycogen found in abundance within the glands, but they do not act as excretory organs for the fats ingested or circulating in the blood. Vitamins, too, have found favor from time to time in the treatment of acne but their role, if any, in relation to the function of the sebaceous glands is not clearly understood.

#### Hormones

The influence of hormones, particularly androgens, on the activity of the pilosebaceous glands and the production of acne has already been mentioned. Yet despite the relationship, treatments to counteract hormone-induced activity of these glands have been tried and found to fail in the majority of cases. In short, there is no reliable form of hormone therapy useful for the prolonged treatment of the comedones and pustules of *ordinary* acne.

## *QUESTIONS AND ANSWERS*

**Q.** *Do you use X-ray therapy in acne?*

**A.** We have not used X-ray for treating acne for many years. There are many opinions about both the benefits and the possible hazards of X-ray therapy. In our opinion, the balance has tipped against X-ray therapy because we think the antibiotics and steroids produce equal or better results with less potential hazards.

**Q.** *You say halogen-containing drugs are detrimental to acne; what about the use of iodized salt?*

**A.** Because even a trace of iodide or bromide can contribute to or even cause acne lesions, such things as iodized salt and bromide headache remedies should be avoided.

# "A multiplicity of complaints . . . a paucity of physical findings"

Thus was a patient's condition described in a 'Compazine' case report. She responded well to 'Compazine'. With her anxiety and apprehension relieved, her complaints promptly ceased.

When you suspect an emotional cause for a patient's ill-defined distress, 'Compazine' provides two valuable services. First, 'Compazine' relieves nervousness and tension. Second, 'Compazine' can provide valuable diagnostic aid. As anxiety and tension are controlled, the extent of emotional involvement can be ascertained and, if necessary, additional therapy begun.

In conditions such as g.i. tension states, cardiac neuroses and menstrual disorders, 'Compazine' often is all that is necessary to bring relief.

For complete prescribing information, see back of magazine.

**Compazine®**

brand of prochlorperazine

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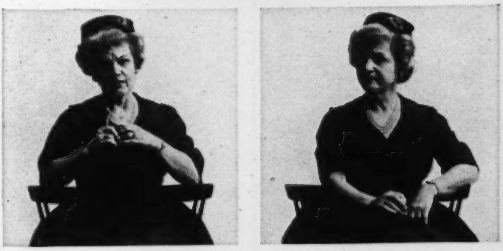
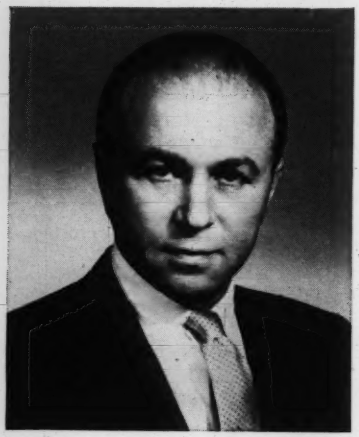


# INTERNAL MEDICINE



**Arnold P. Friedman, M.D.**
**Columbia University**

*Arnold P. Friedman is Associate Professor of Clinical Neurology at the College of Physicians and Surgeons of Columbia University and Physician-In-Charge of the Headache Unit of Montefiore Hospital, New York. He is Associate Attending Physician at the Neurological Institute of Presbyterian Hospital and a consultant in neurology for the Veterans Administration. A member of the American Neurological Association, he is the author of numerous publications on headache including the textbook MODERN HEADACHE THERAPY, and the co-author of HEADACHE: DIAGNOSIS AND TREATMENT.*

## HEADACHE AND SYSTEMIC DISEASE

Headache, one of the most common of all symptoms, is often associated with systemic disease – as an early warning symptom, as part of an exacerbation of disease, or as a continuous feature of the disease's clinical course. Headache may accompany a variety of illnesses; and, it may occur long before, or long after, other symptoms are noted.

The physician dealing with this symptom should consider two aspects of the diagnosis: (1) the pain mechanism and (2) the nature of the underlying disorder. Thus, therapy can be directed toward two aspects of the problem: the symptoms and the basic disease.

The mechanisms by which systemic disease cause headache include: excessive cranial vascular dilatation and distention; inflammatory involvement of pain-sensitive extra- and intracranial structures; direct involvement of the cranial vasculature by disease processes; mechanical distortion of pain-sensitive structures; altered intracranial dynamics; and a variety of mechanisms, including disturbances of physiology as electrolyte imbalance, anaphylactic reactions and metabolic alterations.

Frequently, more than one headache-producing mechanism is in operation during the course of an underlying disease. Present evidence indicates

that systemic disease causes head pain by its secondary effect on cranial physiology and not as "referred pain" from distant organs.

**Diagnostic Considerations**

There are many things about the headache itself that should be considered—the duration of illness, location of attacks, timing of headache attacks, character of the headache, associated manifestations during the headache, and circumstances that surround the onset. Here are some points that are usually significant.

• Generally, a long history of headache tends to eliminate the possibility of intracranial mass and inflammatory lesions and points to vascular and muscle-contracting mechanisms. On the other hand, persistent headaches that have occurred only recently, especially if they occur late in life (for example, in a man of 60), should alert you to suspect some form of structural systemic disease such as metastasis, brain tumor, cranial arteritis, or cervical arthritis.

• The location of headache may be significant. When recurrent headaches strike always in the same site, the possibility of an intracranial anomaly must be considered. Migraine headaches which vary from side to side in different attacks are probably not due to a structural lesion. A change in the location or character of the headache or the development of new symptoms or signs, in a patient who has chronic recurring headaches, may indicate the presence of an unrecognized systemic disease. The latter is also suggested when headache is associated with fever, rashes, joint and muscle pains, jaundice and localized areas of inflammation.

• A description of the headache is not always of diagnostic value, but certain types of headaches do often follow a pattern. A throbbing quality is characteristic of headaches of vascular origin (migraine, hemangiomas, or systemic disease, such as febrile illnesses and toxic states).

• Severity of headache is entirely non-specific and not a reliable indication of the cause. Headache is sometimes mild with advanced and serious intracranial lesions or systemic disease and yet may be intense or disabling when associated with a chronic anxiety state or conversion reaction.

• Any *change* in the pattern of headache in patients with chronic recurring headaches (migraine, tension headaches) such as lack of response to previously effective medication may point to the presence of a structural disease. Thus the migraine patient's failure to respond to ergotamine tartrate may indicate that an aneurysm has been the cause of the periodic recurring headache and that the aneurysm has started to leak.

• Effects of postural changes are sometimes diagnostic. Headache following lumbar puncture usually develops 6 to 20 hours after spinal tap, but occasionally the onset may be delayed for several days. The pain is quite often severe and develops when the patient stands or sits and disappears when he is recumbent. Severe attacks of headache sometimes related to posture may occur with colloid cysts of the third ventricle; the headache is frequently worse when the patient is supine, but is relieved when he is prone, or in knee-chest position. Tumor headache is sometimes worse while the patient is up-

right, but vascular headaches may be lessened.

• Time of occurrence may also be significant. Headaches associated with hypertension may begin early in the morning. However, headaches of the tension type associated with sustained cervical and cranial muscular contraction may occur in the hypertensive at any time of the day or night and alternate with the early morning headache. In acute frontal sinusitis, headache usually begins in the morning and gradually ends toward evening.

• Most headaches have a gradual onset. The exceptions are those due to intracranial hemorrhage due to rupture of a cerebral artery, or of a saccular or arteriovenous aneurysm.

### Clues from the History

A history of head injuries, cardiac abnormalities, rheumatic fever, anemia, nephritis, malignant growths, congenital abnormalities, and malaria may point to the cause. So may the patient's background, such as a family history of diabetes, pernicious anemia, hypertension, migraine, and mental illness. Information about the patient's work may help by revealing exposure to nitrates, carbon tetrachloride, benzene, carbon monoxide, and other toxic chemicals. And, information about recent travel, exposure to tropical diseases, to high altitude, or to unusual or allergenic food, may help in diagnosis.

### Associated Signs

Associated signs are an important aid in diagnosis. For example, disturbances of vision may occur in migraine, brain tumor, aneurysm and glaucoma. The visual disturbances of migraine usually precede the headache, except for photophobia which often accompanies the headache proper.

The presence of varying central-nervous-system signs helps differentiate brain tumor and aneurysm. In glaucoma, there are increased intraocular tension and defects in the visual fields and color vision.

In the post-traumatic syndrome, headache is frequently associated with transient or lengthy episodes of dizziness that are usually produced by change in posture. Headaches associated with brain tumors may also be accompanied by vertigo or feelings of unsteadiness. Occasionally, headaches are associated with the vertigo of Menière's syndrome.

Headache associated with peripheral or cranial nerve paralysis, respiratory or swallowing difficulties, should alert you to a more serious turn of events in the clinical picture. The presence of headache with transient episodes of neurologic deficit should suggest the possibility of an insufficiency syndrome of the carotid, vertebral, and basilar artery systems. The importance of headache in these conditions is that it may alert you to a situation which may result in total occlusion.

Gastrointestinal symptoms are typically associated with migraine headaches. However, such disturbances as anorexia, nausea or vomiting can accompany any severe headache.

### Physical Examination

A thorough examination of the patient including physical and neurological examination and laboratory studies, will be of valuable diagnostic aid in recognizing factors which may produce headache.

Direct attention to the skull should be a routine part of the examination, but is seldom of diagnostic value. However, during a migraine attack it may reveal the enlarged and strongly pulsating scalp artery or the tender pulseless vessels and localized erythema of temporal or cranial arteries. Rarely, auscultation reveals an underlying angioma when a bruit is heard. During muscle-contraction headache, tautness and tenderness of nuchal muscles and trapezii may be evident. But these signs are difficult to evaluate.

If you find enlarged lymph nodes or an enlarged spleen, consider the possibility of a blood dyscrasia or lymphoma which may be associated with extradural invasion in the cervical region. Atypical lymphocytes may implicate infectious mononucleosis as the cause of headache. A differential blood count and sedimentation rate may explain a recurring headache which for long periods may be the only manifestation of infection such as brucellosis, hepatitis without jaundice, chronic malaria, subacute bacterial endocarditis, or blood dyscrasias. Examine the fundi, because changes in the retina or optic nerve may occur in the course of diseases such as hypertension, chronic nephritis, diabetes mellitus, leukemia, polycythemia, syphilis, and generalized arteriosclerosis—all of which may be associated with headache.

In pulmonary states associated with both anoxia and carbon dioxide retention, headache may be associated with papilledema and mental symptoms that may simulate brain tumor; in such patients, the use of oxygen further depresses the respiratory center.

If your patient is hypertensive, remember that the presence or severity of headache is not necessarily related to the level of the blood pressure. Sometimes, migraine sufferers experience an exacerbation of headache if they develop hypertension. Rarely, severe bouts of headache associated with hypertension, palpitation, tachycardia, sweating and anxiety may result from a pheochromocytoma.

You may find it useful to evaluate the patient's response to vasodilators and vasoconstrictors. The occurrence of headaches upon use of vasodilator, with relief by a vasoconstrictor, suggests a vascular mechanism.

Sometimes ancillary tests may prove of diagnostic significance. X-rays of the head are usually indicated in most patients with headache. When suboccipital or nuchal pain is prominent, x-rays of the cervical spine should be included. Electroencephalography is indicated when there is reasonable suspicion of intracranial structural disease. Allergy tests are worth considering only when the history offers leads in this direction.

Management of the patient with headache affected with systemic disease consists of control of the primary disease, an attack upon the headache mechanism, the administration of analgesic drugs, and reduction of emotional tension and anxiety. Unless contraindicated, the combination of a non-narcotic analgesic with a tranquilizer or sedative is more effective therapy than use of an analgesic alone. In combination, these drugs affect not only the pain threshold but the reaction to suffering.

Of 39 women treated for long-term infertility with 'Cytomel'

18 became pregnant

13 with amenorrhea began to menstruate regularly

From a report by Foster, H.M.: Am. J. Obst. & Gynec. 77:130 (Jan.) 1959.

# CYTOMEL®

brand of liothyronine

**ADMINISTRATION AND DOSAGE:** Dosage should be adjusted according to the severity of the condition and the response of the patient.

Most patients should be started on 25 mcg. of 'Cytomel' daily. To increase dosage to recommended maintenance levels for these patients, increments of 12.5 or 25 mcg. may be made in the daily dosage at intervals of one or two weeks. Dosages in the range of 100 mcg. daily, and higher, are well tolerated by many patients.

When starting dosage is 5 mcg. daily (as in myxedema, male infertility, simple goiter and in patients being switched from thyroid, L-thyroxine, or thyroglobulin), increments of 5 or 10 mcg. may be made in the daily dosage at intervals of one or two weeks. When dosage reaches 25 mcg. daily, increase as described above.

'Cytomel' is usually administered in divided doses.

Note: In geriatric patients or in children always start with 5 mcg. daily and adjust dosage in increments no greater than 5 mcg.

| Indication | Recommended Starting Dose | Recommended Maintenance Dose |
|---|---|---|
| Hypometabolism<br>Mild Hypothyroidism | 25 mcg. daily | 25-75 mcg. daily<br>(Smaller doses may be fully effective in some patients.) |
| Myxedema | 5 mcg. daily | 50-100 mcg. daily |
| Female Reproductive Disorders | 25 mcg. daily | 25-50 mcg. daily |
| Male Infertility<br>(Based on sperm count or sperm motility responses after two to four weeks of treatment at a given dosage level, the daily dosage may be increased by 5 or 10 mcg. If after further treatment the desired response has still not been obtained, the daily dosage may again be increased. Although total daily dosage usually need not exceed 25 mcg., as much as 50 mcg. daily may be used if necessary.) | 5 mcg. daily | 10-25 mcg. daily |
| Simple (non-toxic) Goiter | 5 mcg. daily | 25-75 mcg. daily |

**SPECIAL CONSIDERATIONS AND CAUTIONS:** Tachycardia, excitability, headache, or excessive sweating are signs of overdosage. Medication should be interrupted until the unpleasant symptoms disappear, and then resumed in smaller doses. Since the return to pretreatment status is rapid, 'Cytomel' can usually be resumed at the desired dosage after one to two days.

When a subnormal BMR exists as part of the clinical syndrome of hypometabolism or hypothyroidism, administration in excessive dosage will cause elevation of BMR to levels above normal.

'Cytomel', unlike various forms and fractions of thyroid, will not cause elevation of the blood protein iodine level.

Endogenous thyroid gland function, reflected particularly by $I^{131}$ uptake, may be depressed by 'Cytomel' administration. Depression of this function is most apt to occur with higher dosages (greater than 75 mcg. daily). Experience to date indicates that this effect is not clinically harmful. There have been no unfavorable sequelae in reported instances where 'Cytomel' therapy has been discontinued after depression of $I^{131}$ uptake occurred. In such cases this function has promptly returned to normal after discontinuance of 'Cytomel'.

Since 'Cytomel' is physiologically related to thyroxine, it is not recommended for use in the presence of angina pectoris, in other cardiovascular disorders, or ischemic states. However, if it is used in the presence of such conditions, the starting dosage should never be more than 5 mcg. daily. If dosage is increased, it should be in increments of no more than 5 mcg. daily at approximately two-week intervals.

Hypopituitarism, morphologic hypogonadism and nephrosis should be ruled out before 'Cytomel' is administered.

**CONTRAINDICATION:** Addison's disease.

**FORMULA:** Each 'Cytomel' tablet contains 5 mcg. or 25 mcg. of liothyronine (L-triiodothyronine or LT3), as the sodium salt; 25 mcg. of 'Cytomel' is calorigenically equivalent to approximately 1 gr. of thyroid.

**AVAILABLE IN TWO DOSAGE STRENGTHS:** 25 mcg. (scored) tablets in bottles of 100 and 1000; 5 mcg. tablets in bottles of 100.

Prescribing information adopted Jan. 1961

SK&F Smith Kline & French Laboratories

# SPECIAL FEATURE

**Milton Plotz, M.D.**
**State University of New York**

*Milton Plotz is Clinical Professor of Medicine at the State University of New York, Downstate Medical Center. He is Attending Physician to the Kings County, Brooklyn State, and Long Island College Hospitals and consulting cardiologist to several other hospitals in the New York area. He has contributed many articles in the field of cardiology and internal medicine, and is the author of* CORONARY HEART DISEASE *(Paul B. Hoeber).*

# THE RESTRICTED-SALT DIET: A NEW LOOK

The restricted-sodium diet continues to be one of the most effective methods of therapy for edema. The advent of more and more satisfactory diuretics has not made dietary measures obsolete. On the contrary, it has accentuated the importance of properly selecting cases and maintaining a balance between drug and dietary measures when diuretics are used.

There has been a deplorable trend toward the "free sodium" diet when the patient takes the newer diuretics. Overlooked is the fact, known to every experienced cardiologist, that many patients with mild congestive failure can be treated satisfactorily with salt restriction, alone or more often together with digitalis. Usually these people have mild evidences of water retention, edema or breathlessness on exertion, or may be expected to have such complaints soon (subclinical decompensation). It is easier to handle these patients without worrying about the possible hazards of potassium depletion or the toxicity of diuretics. It is also a comfort to the clinician that almost never will he encounter dangerously low blood-sodium levels with such therapy.

A larger group of cardiac patients are those who cannot be comfortable without diuretics, oral or parenteral. In this category too, curtailment of the ingested sodium is an advantage. It enables the physician to prescribe the least possible amount of diuretic and avoid the complications of diuretic therapy. A good example, which is fairly common, is the patient with both cardiac decompensation and gout. Here the frequently used thiazides will induce serum uric acid

elevation with the possibility of producing unpleasant bouts of gout. On the other hand, where really large amounts of diuretic agents are needed, the diet must, of course, be liberalized.

### Enhancing Taste of Foods

Most patients, and many doctors, make the mistake of regarding the "low salt" diet as a "low spice" diet. This is an error which will deprive the patient of variety and of the pleasure of many tasty dishes. The following are low-sodium condiments which, judiciously used, will aid the patient (and his wife or housekeeper) immeasurably:

ALLSPICE
ALMOND EXTRACT
BASIL
BAY LEAVES
CARDAMON
CARAWAY
CHILI POWDER
CHOCOLATE
CINNAMON
CLOVE OIL
COCOA
COCOANUT
CURRY POWDER (freshly prepared)
DILL
GARLIC
GINGER
HONEY
HORSERADISH (home prepared)
JAMS
LEMON JUICE
LIME JUICE
MACE
MARJORAM
MUSHROOMS
MUSTARD SEED
NUTMEG
ONION
PAPRIKA
PARSLEY
PEPPER
PEPPERMINT
PIMIENTO
ROSEMARY
SAFFRON
SAVORY
SESAME
SOUR SALT (U.S.P. citric acid)
SUGAR
TARRAGON
THYME
VANILLA
VINEGAR

Several herb dealers are marketing combinations of these as highly satisfactory seasonings for foods. Yeast has been toasted over hickory smoke to produce a powder greatly resembling bacon in flavor.

The diet, with spices added, is no longer complained of as flat, uninteresting, and lacking in character. The patient may still feel that his food lacks tang or "bite". This situation can be largely remedied by the use of Tabasco Sauce, a sharp condiment which, as ordinarily employed, contains negligible amounts of sodium. Angostura bitters may be acceptable to those who prefer the taste. In any case, the salt substitutes now available on the market are very agreeable to many patients, and most have the advantage of containing large amounts of potassium. Some persons will prefer the taste of one product over another, and a few do not like any kind. Most will like salt-free soups, homemade or canned, if the "artificial table salts" are added. In some areas of the country, fresh milk is available from which almost all the sodium is removed. Here, too, the milk becomes richer in potassium, a desirable result. I have found this milk completely indistinguishable in taste and cooking qualities from ordinary milk. In all parts of the country, dried low-sodium milk may be bought.

Low-sodium breads are now available in most large cities or may be ordered by mail. Most patients accept these products, especially if the bread is toasted. They should be warned to keep the bread in the refrigerator since it does not keep well. Many people like salt-free matzos and Italian bread sticks.

### Unsuspected Sources of Salt

Patients should be taught early in their period of training to "read the label". They should learn to avoid all sodium compounds, the glutamate and the bicarbonate as well as the chloride of common table salt. They will find that the labeling required by the government will help them to avoid errors and that many products in which they would least expect to find salt are in fact made with sodium.

Some admonitions are in order. Canned soups and other foods almost all contain salt. Salt is added to some frozen foods. Some so-called salt substitutes contain immense amounts of sodium—celery, garlic, and onion salts and the "flavor improvers", such as Accent, which contain sodium glutamate. Only sodium-free artificial sweeteners should be used.

In this country, many candies contain salt and the patient would do well to read the label. This caution is especially necessary in the case of chocolate, particularly the Dutch process variety. I know of a doctor with low-grade failure due to hypertensive heart disease who precipitated an episode of severe pulmonary edema when he forgot this admonition and consumed a large box of gift chocolates.

Taste may be added to some common vegetables and meat as follows.*

## VEGETABLES

*Asparagus:* Sprinkle with freshly grated nutmeg.

*Broccoli:* Add butter and lemon juice.

*Corn:* Add sugar and freshly ground pepper.

*Carrots:* These should be boiled, the water discarded, and boiled again. Mint, tarragon, or butter and chives can be used to add flavor. Carrots should not be used at all in very restricted diets.

*Cauliflower:* Add butter or cream sauce seasoned with nutmeg.

*Cucumbers:* May be diced and boiled in cream sauce with nutmeg, or sliced raw very thin and then marinated in any vinegar.

*Eggplant:* Peeled, diced, boiled, and drained. Add tomatoes, bay leaf, and oregano.

*Green beans or lima beans:* Add nutmeg or savory and butter.

*Sweet potatoes or yams:* Boil and peel, then bake sliced and covered with a mixture of brown sugar and rum.

*Leeks:* Sprinkle with freshly grated nutmeg.

*Mashed potatoes:* Add freshly grated onion and nutmeg.

*Mushrooms:* Sauté in butter with chopped onion.

*Onion:* Boil with clove and thyme.

*Peas:* Boil in sweetened water, drain, and add butter and chopped or powdered mint.

*String beans:* Marjoram improves the taste greatly.

*Tomatoes:* May be broiled, halved, with butter and a pinch of oregano or basil. May be stewed with bay leaf, onion, and oregano.

## MEATS

*Goulash:* Onion, bay leaf, tomato, sweet paprika, pepper, rosemary leaves or oregano.

*Lamb chops:* Rub chops with pepper and ginger before broiling.

*Roast beef:* Rub meat with pepper and ground ginger. Put one large bay leaf in roasting pan and baste every 15 minutes.

*Veal chops:* Rub chops with pepper and saffron. Brown meat in a little margarine, then add a little water and simmer until done.

*Veal stew:* Onion, bay leaf, powdered mace, celery leaves, and bitters to flavor.

*Reprinted from *The Low-Sodium Diet – Some Methods of Making It More Acceptable with Special Reference to the Use of Bitters*, published in the AMERICAN JOURNAL OF CLINICAL NUTRITION, Vol. 5, Nov.-Dec. 1957, page 618.

# QUESTIONS AND ANSWERS

**Q.** *Does it take a patient long to get used to this diet?*

**A.** No, actually it is one of the easiest diets to get accustomed to. After a difficult week or two, most people get along well. The difficulty is to convince the patient (or his doctor) that losing the taste for salt is no great hardship.

**Q.** *Isn't the diet expensive?*

**A.** Only if the patient depends on storemade "salt-free" foods. For example, canned dietetic soups are relatively dear; homemade soups, very inexpensive. The cheapest restaurant foods (those offered on hot tables) often are smothered in gravies containing huge amounts of salt. Steaks, chops, and fish are easily made to order without salt but usually cost more.

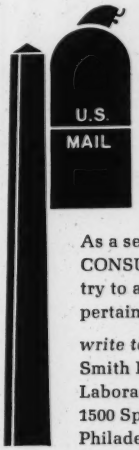
**Q.** *Isn't the diet inconvenient?*

**A.** Yes, a little, if the patient must eat out a good deal. The average worker must find a suitable restaurant or take his meals from home. Actually, any well-stocked cafeteria provides a large choice from which selections can be made. Many salads and all fruits are practically salt free. Persons living alone who must eat most of their meals away from home are at some disadvantage.

**Q.** *Isn't there great risk of the low-salt syndrome taking place?*

**A.** In a temperate climate (like New York's) for the average worker not performing very heavy manual labor in hot weather, the risk of depleting the body sodium is negligible. I have not seen such a case unless diuretics are being given at the same time, in which case extra precaution must be taken.

## CORRESPONDENCE




As a service to readers, CONSULTANT's authors will try to answer any question pertaining to their topics.

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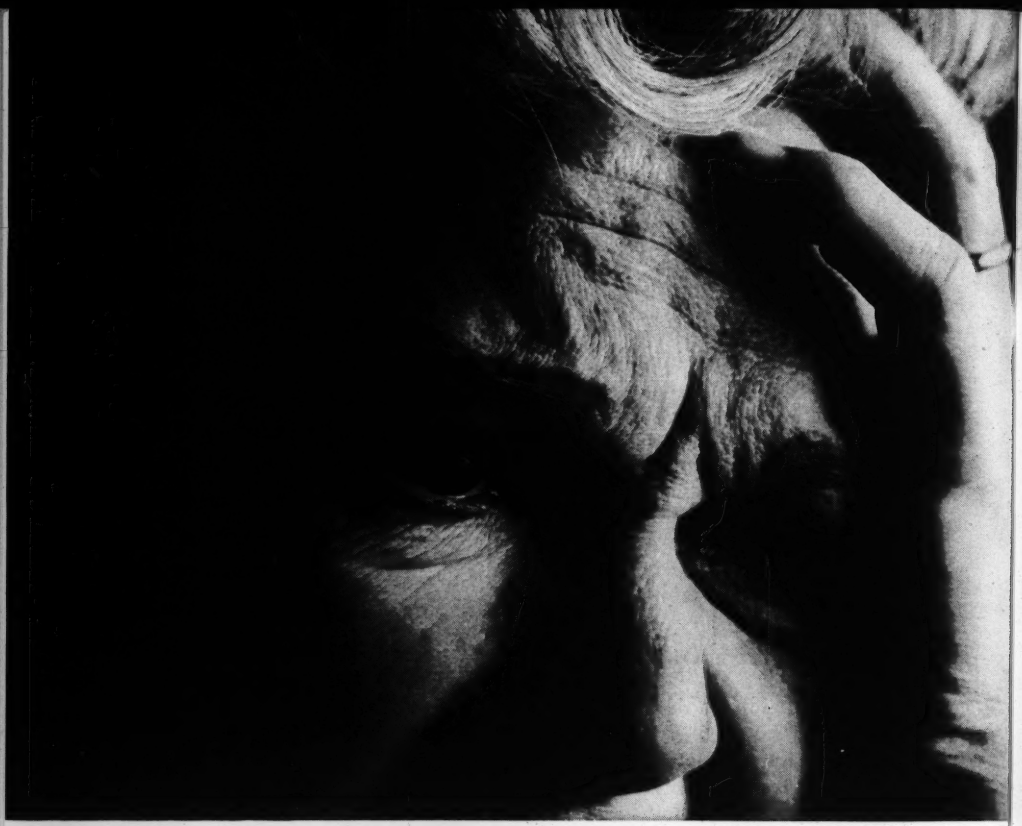

## When your severely anxious patient is "out of range" of mild tranquilizers . . .

For the acutely anxious patient, particularly the patient who is hyperactive, mild tranquilizers frequently fall short.

With 'Thorazine', however, you are giving a tranquilizer that is:

- *profound enough* to control hyperactivity and excitement
- *specific enough* to relieve underlying fear and apprehension
- *flexible enough* so that daily dosage may be raised to substantial levels when required. For example, high daily doses in discharged mental patients are not uncommon.

Long-term studies with 'Thorazine' confirm that in the vast majority of patients the potential benefits of 'Thorazine' far outweigh its possible hazards.

For complete prescribing information, see back of magazine.

**THORAZINE®** a fundamental drug in medicine SK&F

brand of chlorpromazine

Smith Kline & French Laboratories

# THORAZINE®
brand of chlorpromazine

# PRESCRIBING INFORMATION

## Tranquilizer • Antiemetic • Potentiator

The wide diversity of clinical applications in which 'Thorazine' is valuable, as either a specific or an adjuvant, is due to its three fundamental clinical properties: (1) its capacity to alleviate anxiety, tension and agitation without dulling mental acuity, (2) its ability to potentiate sedatives, narcotics and anesthetics, and (3) its profound antiemetic effect.

The tranquilizing effect of 'Thorazine' accounts for its usefulness in somatic conditions where emotional stress is a factor, as well as in mental and emotional disturbances *per se*.

## INDICATIONS

The value of 'Thorazine' is established in the following conditions:

**Moderate to severe mental and emotional disturbances of everyday practice,** particularly those disturbances marked by agitation, tension, apprehension, excitement, or anxiety.

**Somatic conditions complicated by emotional stress,** such as arthritis, tuberculosis, severe tension headaches, gastrointestinal disorders, dermatologic conditions, status asthmaticus and severe asthma.

**Hospitalized psychiatric patients,** to control agitation, dispel delusions and hallucinations, and at the same time to restore or increase the patient's capacity to respond to psychotherapy.

**Nausea, vomiting and hiccups,** with dramatic results in severe and refractory cases.

**Acute or chronic alcoholism,** to control agitation, delirium tremens, and nausea and vomiting.

**Cancer,** as an adjuvant, to control apprehension, suffering due to pain, and nausea and vomiting.

**Intractable pain,** to reduce suffering and to potentiate narcotics or sedatives.

**Obstetrics,** as an adjuvant, to control apprehension, pain, and nausea and vomiting. 'Thorazine' allows a reduction in the amounts of the drugs ordinarily used in obstetrical management, thus lessening the risk of respiratory depression in mother and infant.

**Surgery,** as an adjuvant, to control anxiety and apprehension, pain, and nausea and vomiting; and to reduce by potentiation the amounts of narcotics, sedatives and anesthetics needed.

## ADULT DOSAGE AND ADMINISTRATION

Dosage should always be adjusted to the response of the individual and the severity of the condition. It is important to increase dosage until symptoms are controlled or side effects become troublesome.

**Mental and Emotional Disturbances of Everyday Practice** — Depending on severity, *starting oral dosage* is 10 mg. t.i.d. or q.i.d., or 25 mg. b.i.d. or t.i.d. After a day or two, dosage may be increased by increments of 20 mg. to 50 mg. daily, at semiweekly intervals (increase should be more gradual in emaciated or senile patients) until achieving maximum clinical response. Continue dosage at this level for at least two weeks; then it can usually be reduced to a maintenance level. A daily dosage of 200 mg. is "average," but in some cases, such as discharged mental patients, daily dosages as high as 800 mg. may be necessary. *Starting intramuscular dose* is 25 mg. (1 cc.). If necessary, and if no hypotension occurs, repeat the initial dose in one hour. Subsequent dosages should be oral, starting at 25 mg. to 50 mg. t.i.d.

**Somatic Conditions Complicated by Emotional Stress**—*Starting oral dosage* is 10 mg. to 25 mg. t.i.d. or q.i.d. Increase gradually by 10 mg. to 25 mg. increments at semiweekly or weekly intervals. *Starting intramuscular dosage* is 25 mg. (1 cc.), repeated after one hour if necessary and if no hypotension occurs.

**Hospitalized Psychiatric Patients** — ***Acutely agitated, manic, or disturbed patients:*** *Starting intramuscular dose* is 25 mg. (1 cc.). If no marked hypotension occurs, an additional 25 mg. to 50 mg. injection may be given after one hour. Subsequent intramuscular dosages may be increased gradually over a period of several days — even up to 400 mg. q4-6h in exceptionally severe cases — until the patient is controlled. (In elderly or emaciated patients the dosage should be increased more slowly than in other patients.) Usually the patient becomes quiet and cooperative within 24 to 48 hours after the initial dose, at which time oral doses may gradually be substituted for intramuscular doses (mg. for mg. or higher). Even if control is not complete, oral doses may gradually replace intramuscular doses. During this period, oral dosage should be increased rapidly until the patient is calm. Usually an *oral dose* of 500 mg. a day is sufficient but, if necessary, the dosage may be gradually increased still further to 2,000 mg. a day or higher. ***Less acutely agitated patients:*** *Starting oral dose* is 25 mg. t.i.d. Subsequently, increase the amount gradually until an effective dosage is reached — usually 400 mg. daily is sufficient. ***Duration of therapy:*** It is important to determine the optimal dosage regimen and to continue treatment long enough for maximum clinical response. Maximum improvement is sometimes not apparent until after weeks or even months of therapy.

**Nausea and Vomiting** — *Starting oral dosage* is 10 mg. to 25 mg. q4-6h, p.r.n., and may be increased if necessary. *Starting intramuscular dose* is 25 mg. (1 cc.). If no hypotension occurs subsequent doses of 25 mg. to 50 mg. q3-4h, p.r.n., may be given until vomiting is checked. Then replace intramuscular administration with oral. *Starting rectal dosage* is one 100 mg. suppository q6-8h, p.r.n. In some patients, one-half this dose may be sufficient.

**Hiccups** — *Starting oral dosage* is 25 mg. to 50 mg. t.i.d. or q.i.d. If after 2-3 days symptoms persist, *an intramuscular dosage* of 25 mg. to 50 mg. (1-2 cc.) may be used. *Use intravenous administration* only when symptoms still persist. By slow infusion, 25 mg. to 50 mg. (1-2 cc.) should be administered in 500 cc. to 1,000 cc. of physiologic saline solution, with the patient kept flat in bed. Follow blood pressure closely.

**Alcoholism** — ***Severely agitated patients:*** *Starting intramuscular dose* is 25 mg. to 50 mg. (1-2 cc.). Repeat initial dose if necessary and if no hypotension occurs. Start subsequent oral dosages at 25 mg. to 50 mg. t.i.d. ***Agitated but manageable patients:*** *Starting oral dose* is 50 mg., followed by 25 mg. to 50 mg. t.i.d. ***Ambulatory patients with withdrawal symptoms or sober chronic alcoholics:*** *Starting oral dose* is 10 mg. t.i.d. or q.i.d., or 25 mg. b.i.d. or t.i.d. Patients in a stuporous condition should be allowed to sleep off some of the effects of the alcohol before 'Thorazine' is administered.

**Cancer and Pain** — ***Severe pain:*** *starting intramuscular dosage* is 25 mg. (1 cc.) b.i.d. or t.i.d. ***Milder pain:*** starting oral *dosage* is 10 mg. t.i.d. or q.i.d., or 25 mg. b.i.d. or t.i.d. Because 'Thorazine' potentiates their action, reduce the dosage of narcotics or sedatives to ¼ to ½ of the pre-'Thorazine' level.

**Obstetrics** — *Intramuscular dose* in labor and delivery is 12.5 mg. to 25 mg. (0.5-1 cc.), administered when dilation of the cervix reaches 3 to 5 centimeters or when strong labor is established. At the same time (but not mixed in the syringe with 'Thorazine'), ¼ to ½ the usual dose of a narcotic or sedative and, if desired, 0.4 mg. of scopolamine may be administered. Depending upon blood pressure, respiration and the general condition of the patient, the initial 'Thorazine' dose (alone or with reduced amounts of the other agents) may be repeated in 3 to 5 hours if necessary.

**Surgery** (Adults) — ***Preoperatively,*** *oral dose* is 25 mg. to 50 mg., 2 to 3 hours before the operation. *Intramuscular dose* is 12.5 mg. to 25 mg. (0.5-1 cc.), 1 to 2 hours before the operation. ***During surgery*** 'Thorazine' should be administered only if needed to control nausea and vomiting, retching, hiccups, or other acute symptoms. *Intramuscular dose* is 12.5 mg. (0.5 cc.), repeated in ½ hour if necessary and if no hypotension occurs.

*Intravenous dose* should be no more than 2 mg. per fractional injection, with injections at not less than 2-minute intervals. Also, it should not exceed 25 mg. 'Thorazine' should be diluted to 1 mg./cc. (1 cc. mixed with 24 cc. of physiologic saline solution). *Postoperatively, oral dosage* is 10 mg. to 25 mg. q4-6h, p.r.n. *Intramuscular dosage* is 12.5 mg. to 25 mg. (0.5-1 cc.), repeated in one hour if necessary and if no hypotension occurs.

## PEDIATRIC DOSAGE AND ADMINISTRATION

**Nausea and Vomiting, Behavior Disorders and Pain** – *Oral dosage* is on the basis of ¼ mg./lb. of body weight q4-6h, until symptoms are controlled (i.e., for 40 lb. child–10 mg. q4-6h). Calculate 'Thorazine' Syrup dosage at 10 mg./5 cc. tsp. *Rectal dosage* is on the basis of ½ mg./lb. of body weight q6-8h, p.r.n. (i.e., for 20-30 lb. child–half of a 25 mg. suppository q6-8h). *Intramuscular dosage* is on the basis of ¼ mg./lb. of body weight q6-8h, p.r.n. In children up to 5 years (or 50 lbs.)–not over 40 mg./day. In children 5-12 years (or 50-100 lbs.)–not over 75 mg./day.

**Pain**–Because 'Thorazine' potentiates the action of narcotics and sedatives, reduce the dosage of these agents to ¼ to ½ of the pre-'Thorazine' level.

**Behavior Disorders**–In severe cases, 50-100 mg. daily has been used and, in older children, 200 mg. or more daily may be required.

**Surgery (Children)** – *Preoperatively*, dose is on the basis of ¼ mg./lb. of body weight given either orally 2 to 3 hours before the operation, or intramuscularly 1 to 2 hours before. *During surgery*, the dose is on the basis of ⅛ mg./lb. of body weight, repeated in ½ hour if necessary and if no hypotension occurs. The intravenous dose should be no more than 1 mg. per fractional injection, with injections at not less than 2-minute intervals. Intravenous dosage during surgery should not exceed recommended intramuscular dosage and should always be diluted to 1 mg./cc. *Postoperatively*, dosage is on the basis of ¼ mg./lb. of body weight, either orally q4-6h, p.r.n., or intramuscularly, a single dose repeated in one hour if necessary and if no hypotension occurs.

## NOTES ON PARENTERAL ADMINISTRATION

Except for acute ambulatory cases, parenteral administration should generally be reserved for bedfast patients. Parenteral administration should always be made with the patient lying down and remaining so for at least ½ hour afterward because of possible hypotensive effects. The injection should be given *slowly, deep* into the upper outer quadrant of the buttock. If irritation and pain at the site of injection are problems, dilution of 'Thorazine' Injection with physiologic saline solution or 2% procaine solution may be helpful. Subcutaneous administration is not advisable, and care should be taken to avoid injecting undiluted 'Thorazine' Injection into a vein. Intravenous administration is recommended only for severe hiccups and surgery.

Because contact dermatitis has been reported, avoid getting the solution on hands or clothing.

## SIDE EFFECTS

The drowsiness caused by 'Thorazine' may be unwanted in some patients. It is usually mild to moderate and disappears after the first or second week of therapy. If, however, drowsiness is troublesome, it can usually be controlled by lowering the dosage or by administering small amounts of dextro amphetamine.

Other side effects that have been reported occasionally are dryness of the mouth, nasal congestion, some constipation, miosis in a few patients and, very rarely, mydriasis. Mild fever (99°F.) may occur occasionally during the first days of therapy with large intramuscular doses. During 'Thorazine' therapy some patients have an increased appetite and gain weight. Usually these patients reach a plateau beyond which they do not gain further weight.

## CAUTIONS

**Jaundice:** In the more than 14 million patients who have been treated with 'Thorazine' in the United States, the incidence of jaundice–regardless of indication, dosage, or mode of administration–has been low. Few cases have occurred in less than one week or after six weeks. Jaundice due to 'Thorazine' is of the so-called "obstructive" type; is without parenchymal damage; and is usually promptly reversible upon the withdrawal of 'Thorazine'. Because detailed liver function tests of 'Thorazine'-induced jaundice give a picture which mimics extrahepatic obstruction, exploratory laparotomy should be withheld until sufficient studies confirm extrahepatic obstruction.

**Agranulocytosis:** Agranulocytosis, although rare, has been reported in patients on 'Thorazine' therapy. Patients receiving 'Thorazine' should be observed regularly and asked to report at once the sudden appearance of sore throat or other signs of infection. If white blood counts and differential smears give an indication of cellular depression, the drug should be discontinued, and antibiotic and other suitable therapy should be instituted. Because most reported cases have occurred between the fourth and the tenth weeks of treatment, patients on prolonged therapy should be observed particularly during that period.

A moderate suppression of total white blood cells is sometimes observed in patients on 'Thorazine' therapy. If not accompanied by other symptoms, it is not an indication for discontinuing 'Thorazine'.

**Potentiation:** 'Thorazine' prolongs and intensifies the action of many central nervous system depressants, such as barbiturates and narcotics. Consequently, it is advisable to stop administration of such depressants before initiating 'Thorazine' therapy. Later the depressant agents may be reinstated, starting with low doses, and increasing according to response. Approximately ¼ to ½ the usual dosage of such agents is required when they are given in combination with 'Thorazine'. (However, 'Thorazine' does not potentiate the anticonvulsant action of barbiturates. In patients who are receiving anticonvulsants, the dosage of these agents–including barbiturates–should not be reduced if 'Thorazine' is started. Rather, 'Thorazine' should be started at a very low dosage and increased, if necessary.)

**Hypotensive Effect:** Postural hypotension and simple tachycardia may be noted in some patients. In these patients, momentary fainting and some dizziness are characteristic and usually occur shortly after the first parenteral dose, occasionally after a subsequent parenteral dose–very rarely after the first oral dose. In most cases, prompt recovery is spontaneous and all symptoms disappear within ½ to 2 hours with no subsequent ill effects. Occasionally, however, this hypotensive effect may be more severe and prolonged, producing a shock-like condition. In consideration of possible hypotensive effects, the patient should be kept under observation (preferably lying down) for some time after the initial parenteral dose. If, on rare occasions, hypotension does occur, it can ordinarily be controlled by placing the patient in a recumbent position with head lowered and legs raised. If it is desirable to administer a vasoconstrictor, 'Levophed' and 'Neo-Synephrine'★ are the most suitable. Other pressor agents, including epinephrine, are not recommended because phenothiazine derivatives may reverse the usual elevating action of these agents and cause a further lowering of blood pressure.

**Antiemetic Effect:** The physician should always bear in mind that the antiemetic effect of 'Thorazine' may mask signs of overdosage of toxic drugs and may obscure diagnosis of conditions such as intestinal obstruction and brain tumor.

**Dermatological Reactions:** Dermatological reactions have been reported. Most have been of a mild urticarial type, suggesting allergic origin. Some of them appear to be due to photosensitivity, and it is advisable that patients on 'Thorazine' avoid undue exposure to the summer sun.

**Neuromuscular Reactions:** With very large doses of 'Thorazine', as frequently used in psychiatric cases over long periods, there have been a few patients who have exhibited neuromuscu-

★'Levophed' and 'Neo-Synephrine' are the trademarks (Reg. U.S. Pat. Off.) of Winthrop Laboratories for its brands of levarterenol and phenylephrine respectively.

lar reactions (extrapyramidal symptoms) which closely resemble parkinsonism. Such symptoms are reversible and usually disappear within a short time after the dosage has been decreased or the drug withdrawn. These neuromuscular reactions can also be controlled by the concomitant administration of standard anti-parkinsonism agents.

**Lactation:** Moderate engorgement of the breast with lactation has been observed in female patients receiving very large doses of 'Thorazine'. This, however, is a transitory condition which disappears on reduction of dosage or withdrawal of the drug.

## CONTRAINDICATIONS

In comatose states due to central nervous system depressants (alcohol, barbiturates, narcotics, etc.), and also in patients under the influence of large amounts of barbiturates or narcotics.

## AVAILABLE

**Tablets,** 10 mg., 25 mg., 50 mg. and 100 mg., in bottles of 50, 500 and 5000; 200 mg., for use in mental hospitals, in bottles of 500 and 5000. (Each tablet contains chlorpromazine hydrochloride, 10 mg., 25 mg., 50 mg., 100 mg., or 200 mg.)

**Ampuls,** 1 cc. and 2 cc. (25 mg./cc.), in boxes of 6, 100 and 500. (Each cc. contains, in aqueous solution, chlorpromazine hydrochloride, 25 mg.; ascorbic acid, 2 mg.; sodium bisulfite, 1 mg.; sodium sulfite, 1 mg.; sodium chloride, 6 mg.)

**Multiple-dose Vials,** 10 cc. (25 mg./cc.), in boxes of 1, 20 and 100. (Each cc. contains, in aqueous solution, chlorpromazine hydrochloride, 25 mg.; ascorbic acid, 2 mg.; sodium bisulfite, 1 mg.; sodium sulfite, 1 mg.; sodium chloride, 1 mg. Contains benzyl alcohol, 2%, as preservative).

**Spansule® capsules,** 30 mg., 75 mg., 150 mg. and 200 mg., in bottles of 30, 250 and 1500; also 300 mg., in bottles of 30 and 1500. (Each 'Spansule' capsule contains chlorpromazine hydrochloride, 30 mg., 75 mg., 150 mg., 200 mg., or 300 mg.)

**Syrup,** 10 mg./teaspoonful (5 cc.), in 4 fl. oz. bottles. (Each 5 cc. contains chlorpromazine hydrochloride, 10 mg.)

**Suppositories,** 25 mg. and 100 mg., in boxes of 6. (Each suppository contains chlorpromazine, 25 mg. or 100 mg.; glycerin, glyceryl monopalmitate, glyceryl monostereate, hydrogenated cocoanut oil fatty acids, hydrogenated palm kernel oil fatty acids, lecithin.)

**Concentrate** (for hospital use), 30 mg./cc., in 4 fl. oz. bottles, packages of 12 and 36; and in 1 gal. bottles. (Each cc. contains chlorpromazine hydrochloride, 30 mg.)

Prescribing information adopted January, 1961

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# COMPAZINE®

brand of prochlorperazine

# PRESCRIBING INFORMATION

### Antiemetic • Tranquilizer

'Compazine' provides a beneficial calming effect and prompt antiemetic action with unusual freedom from drowsiness and depressing effect. Clinical experience in several million patients has shown 'Compazine' to be promptly effective in low dosage, with minimal side effects in the dosage range recommended for everyday practice.

## INDICATIONS

*1. **Anxiety, tension, agitation,*** confusion, chronic alcoholism and behavior disorders in children.

*2. **Emotional stress associated with somatic conditions*** such as g.i. disorders, cardiovascular conditions, hypertension, menopause, premenstrual tension, neurodermatitis, arthritis, asthma, cancer, tuberculosis and tension headache.

*3. **Nausea and vomiting of widely varying causes*** such as pregnancy, postoperative conditions, viral gastroenteritis and other infectious conditions, irradiation therapy and motion sickness. In most patients, relief is provided within a short time after one oral dose.

*4. **In surgery and obstetrics*** to prevent or control: (a) nausea, vomiting and retching; and (b) fear, tension and restlessness.

*5. **In psychiatry*** to control agitation, anxiety, tension and confusion that may be seen in psychotic states.

## ADMINISTRATION AND USUAL DOSAGE

Dosage should be determined according to the severity of the condition and the response of the patient. It is important to begin therapy with the lowest recommended dosage. In hospitalized patients or those under adequate supervision, higher doses may be indicated.

## USUAL ADULT DOSAGE

**Tablets:** The usual starting dosage is 5 mg. three or four times daily. Some patients will respond better when subsequent dosage is raised to 10 mg. t.i.d. or q.i.d. Dosage over 40 mg. daily should be used only in resistant cases.

**Spansule® sustained release capsules:** The usual starting dosage is one 15 mg. 'Spansule' capsule taken upon arising, or one 10 mg. 'Spansule' capsule in the morning and evening. Some patients may subsequently require dosage increased to one 30 mg. capsule in the morning. Dosage over 40 mg. daily should be used only in resistant cases. (B.i.d. dosage of the 30 mg. capsule should be limited to severe cases.)

Dosage recommendations for other oral forms of 'Compazine' may be applied to 'Compazine' *Spansule* capsules on the basis of the total daily dose in milligrams. (For example: one 15 mg. 'Compazine' *Spansule* capsule replaces 5 mg. 'Compazine' Tablets, t.i.d.) All strengths have the same *duration* of action. They differ only in *intensity* of therapeutic effect.

*In "morning sickness" of pregnancy,* one 'Compazine' *Spansule* capsule taken before retiring affords antiemetic activity throughout the night and into the morning, thus protecting against "morning sickness."

The 15 mg. 'Compazine' *Spansule* capsule is ideal for once-a-day administration. The 10 mg. 'Compazine' *Spansule* capsule is ideal for twice-a-day (q12h) administration.

**Syrup:** 5 mg. to 10 mg. (1 to 2 teaspoonfuls) three or four times daily.

**Suppositories:** Usual dosage in adults is one 25 mg. 'Compazine' Suppository twice daily.

**Injection:** Total parenteral dosage in 24 hours should not exceed 40 mg.

***For intramuscular administration,*** an initial dose of 5 mg. to 10 mg. (1 to 2 cc.) of 'Compazine' Injection should be injected *deeply* into the upper outer quadrant of the buttock. Repeat, if necessary, at intervals of 3 to 4 hours. Pain at the site of injection has not been a problem. ***For intravenous administration,*** see surgery section. Dilution is not required. ***Subcutaneous administration*** is not advisable because of local irritation.

It is recommended that 'Compazine' Injection not be mixed with other agents in the syringe.

Dermatitis due to contact with 'Compazine' has not been a problem. However, it is recommended that nurses or others giving frequent injections take precautions to avoid getting the solution on their hands or clothing.

'Compazine' Injection should be protected from light, since exposure may cause discoloration. Slight yellowish discoloration will not significantly alter the potency or therapeutic efficacy. However, if markedly discolored, the solution should be discarded.

## IN SURGERY (Adults)

| ROUTE | DOSAGE |
|---|---|
| ***preoperatively*** | |
| Intramuscular injection | 5 mg. to 10 mg. (1-2 cc.) |

1 to 2 hours before induction of anesthesia. Repeat once in 30 minutes if necessary.

| ROUTE | DOSAGE |
|---|---|
| Intravenous injection | 5 mg. to 10 mg. (1-2 cc.) |

15 to 30 minutes before induction of anesthesia.

| | |
|---|---|
| Intravenous infusion | 20 mg. (4 cc.) per liter of isotonic solution |

Add to I.V. infusion 15 to 30 minutes before induction. Repeat once if necessary.

*during surgery*

| | |
|---|---|
| Intramuscular or Intravenous injection | 5 mg. to 10 mg. (1-2 cc.) |

When needed to control acute symptoms. Repeat once if necessary.

*postoperatively*

*To prevent* anxiety, nausea, vomiting, or emergence excitement, add to I.V. infusion: 20 mg. (4 cc.) per liter of isotonic solution.

*For immediate control* of acute nausea, vomiting, retching, or emergence excitement, inject 5 mg. to 10 mg. (1-2 cc.), I.V. or I.M. Repeat once if necessary.

## IN OBSTETRICS

'Compazine' dosage should be adjusted to the individual patient and her condition in accordance with the general use of the drug (i.e., 5 mg. to 10 mg. per dose; 15 mg. to 40 mg. per day). The following dosage suggestions should prove satisfactory for the majority of obstetric patients.

***To relieve anxiety or prevent vomiting during the first stage of labor,*** the usual dosage is 10 mg. of 'Compazine' by intramuscular injection. As labor progresses, or if it is prolonged, subsequent 10 mg. doses may be administered as needed. The total daily dose need rarely exceed 30 mg.

***To control postpartum anxiety or nausea and vomiting,*** the usual total daily dose of 'Compazine' is 15 mg. to 30 mg. administered orally or intramuscularly.

NOTE: 'Compazine' has no clinically significant potentiating effect on narcotics, anesthetics, or sedatives. However, because the 'Compazine' patient is calm and relaxed, it is sometimes possible to produce satisfactory analgesia with less than the customary amounts of these agents. This lack of potentiating effect also minimizes the risk of intensifying or prolonging the effect of residual anesthetics and other depressant agents used in surgery or labor and delivery.

As with intravenous administration of any surgical or obstetric adjuvant, the increased possibility of hypotension should be kept in mind if 'Compazine' is administered by either intravenous injection or infusion.

## USUAL CHILDREN'S DOSAGE

It is important always to use the lowest effective dosage, because as dosage is raised the possibility of side effects increases. There have been occasional cases of neuromuscular reactions (extrapyramidal symptoms) in children. These have been transitory and reversible.

**Nausea and vomiting** are usually controlled during the first day of therapy. Therefore more than one day's therapy is seldom necessary.

| Weight | Dosage | Not to exceed |
|---|---|---|
| Under 20 lbs. | not recommended | |
| 20-29 lbs. | 2.5 mg. once or twice a day | 7.5 mg. per day |
| 30-39 lbs. | 2.5 mg. b.i.d. or t.i.d. | 10.0 mg. per day |
| 40-85 lbs. | 2.5 mg. t.i.d. or 5 mg. b.i.d. | 15.0 mg. per day |

**For behavior disorders,** dosage may be increased gradually, if necessary, within the following daily limits:

2 to 6 years of age: Total daily dose should not exceed 20 mg.
6 to 12 years of age: Total daily dose should not exceed 25 mg.

**For rapid control of nausea and vomiting or behavior disorders:**

*Injection:* For children under 12 years of age, each dose should be calculated on the basis of 0.06 mg. of 'Compazine' per pound of body weight and should be administered by deep intramuscular injection. For example, a 40-pound child would receive an injection of 2.5 mg. (0.5 cc.). Control is usually obtained with a single dose.

## 'COMPAZINE' IN PSYCHIATRY

'Compazine' is indicated for control of agitation, anxiety, tension and confusion that may be seen in such conditions as schizophrenias; manic-depressive states, manic phase; severe personality disorders; involutional psychoses; degenerative conditions; and senile psychoses.

### ADULTS

**Oral psychiatric dosage:** *In relatively mild conditions,* as may be seen in private psychiatric practice or on outpatient clinics, the suggested starting dosage is 5 mg. t.i.d. or q.i.d. Some patients will respond better when subsequent dosage is raised to 10 mg. t.i.d. or q.i.d. *In moderate or severe conditions,* when patients are either hospitalized or under adequate supervision, the suggested starting dosage is 10 mg. t.i.d. or q.i.d. Dosage should be increased gradually until symptoms are controlled or side effects become bothersome. Experience has shown that when dosage is increased gradually (by small increments every two or three days) side effects either do not occur or are easily controlled.

Some patients will obtain satisfactory results on 50 mg. to 75 mg. of 'Compazine' daily. In more severe disturbances, the optimum dosage in most patients is 100 mg. to 150 mg. daily. With oral administration, response ordinarily becomes evident within a day or two. Longer periods of treatment are usually required before maximal improvement is obtained.

**I.M. psychiatric dosage:** For immediate control of severely disturbed adult patients, an initial dose of 10 mg. to 20 mg. (2-4 cc.) should be injected deeply into the upper outer quadrant of the buttock. If necessary, this dose should be repeated every 2 to 4 hours to gain control of the patient. Patients often respond shortly after the first injection. In resistant cases, the initial dose may be repeated hourly. More than three or four doses are seldom necessary. If, in rare cases, parenteral medication is indicated over a prolonged period, 10 mg. to 20 mg. (2-4 cc.) at 4- to 6-hour intervals is the usual dosage. Pain and irritation at the site of injection have rarely been encountered and some patients have been given the drug intramuscularly for periods of several weeks. After control is achieved by intramuscular administration, most patients can be switched to an oral form of the drug at the same dosage level or higher.

### CHILDREN *(2 to 12 years)*

**Oral psychiatric dosage:** The suggested children's starting dosage in psychiatry is 2.5 mg. (½ teaspoonful of syrup) two or three times daily, or 5 mg. (one teaspoonful of syrup or one 5 mg. tablet) twice daily, according to body weight. During the first day, the total daily dose should not exceed 10 mg. Dosage is then increased according to the patient's response. (2.5 mg. and 5 mg. suppositories are also available.)

*For ages 2 to 6,* the total daily dosage usually does not exceed 20 mg. *For ages 6 to 12,* the total daily dosage usually does not exceed 25 mg. Because extrapyramidal symptoms have been reported in children as well as in adults, it is important to use the lowest effective dosage.

## SIDE EFFECTS

In the dosage range recommended for everyday practice, side effects have been infrequent, transitory and usually mild. A few patients may experience a mild drowsiness when first taking 'Compazine'. There may also be occasional cases of dizziness,

skin reaction and neuromuscular reactions (extrapyramidal symptoms); rarely, hypotension.

*Neuromuscular Reactions*

Occasionally, neuromuscular reactions (extrapyramidal symptoms) have been observed with 'Compazine' therapy. It is important, therefore, to use the lowest effective dosage, because as dosage is raised the possibility of these reactions increases.

***Motor Restlessness:*** A few patients on 'Compazine'—particularly those in whom dosage has been raised to higher levels—may experience a transient unpleasant stimulation or jitteriness, characterized by restlessness and insomnia. The dosage of 'Compazine' should not be increased while these side effects are present. Patients should be reassured that such effects are temporary and will disappear spontaneously. In those cases where the symptoms are particularly bothersome, reduction of dosage or the concomitant administration of a sedative may be helpful.

***Dystonias:*** These neuromuscular reactions are seen in a significant percentage of hospitalized mental patients on high dosages. The muscles of the face and shoulder girdle may be selectively involved. Symptoms observed have included spasm of the neck muscles, extensor rigidity of back muscles, carpopedal spasm, eyes rolled back, trismus and swallowing difficulty. Despite some similarity to symptoms of serious neurologic disorders, these reactions are usually promptly reversible by temporary discontinuance of 'Compazine' therapy and administration of a sedative such as phenobarbital. The dosage and route of administration should be determined according to the severity of the symptoms. Patients should be reassured that the symptoms are transitory. Depending on the severity of the dystonia, suitable supportive measures, such as maintaining a clear airway and adequate hydration, should be employed. Note: It has been reported that injectable administration of Benadryl* may also be helpful.

***Pseudo-parkinsonism:*** These neuromuscular reactions may resemble the classic parkinsonism syndrome. Treatment should include temporary discontinuance of 'Compazine' therapy and the administration of any standard anti-parkinsonism agent (see *PDR*). Patients should also be reassured that these symptoms are transitory. Depending on the severity of symptoms, suitable supportive measures, such as maintaining a clear airway and adequate hydration, should be employed.

## CAUTIONS

Clinical experience has demonstrated that 'Compazine', a phenothiazine derivative, has a wide margin of safety and that there is little likelihood of blood or liver toxicity. The physician should be aware, however, of their possible occurrence.

The antiemetic action of 'Compazine' may mask signs of overdosage of toxic drugs or may obscure the diagnosis of conditions such as intestinal obstruction and brain tumor.

'Compazine' has no clinically significant potentiating action. However, if depressant agents are used in conjunction with this drug, the possibility of an additive effect should be kept in mind.

## CONTRAINDICATIONS

'Compazine' is contraindicated in comatose or greatly depressed states due to central nervous system depressants.

## AVAILABLE

There is a dosage form of 'Compazine' for every medical need. Tablets, 5 mg. and 10 mg. and, for use in psychiatry, 25 mg., in bottles of 50, 500 and 5000. Each tablet contains 5 mg., 10 mg., or 25 mg. of prochlorperazine as the dimaleate.

'Spansule' capsules, 10 mg., 15 mg. and 30 mg., in bottles of 30, 250 and 1500; and, for use in psychiatry, 75 mg., in bottles of 30 and 1500. Each capsule contains 10 mg., 15 mg., 30 mg., or 75 mg. of prochlorperazine as the dimaleate.

Ampuls, 2 cc. (5 mg./cc.), in boxes of 6, 100 and 500. Each cc. contains, in aqueous solution: 5 mg. prochlorperazine as the ethanedisulfonate, 1 mg. sodium sulfite, 1 mg. sodium bisulfite, 8 mg. sodium phosphate and 12 mg. sodium biphosphate.

Multiple-dose Vials, 10 cc. (5 mg./cc.), in boxes of 1, 20 and 100. Each cc. contains, in aqueous solution: 5 mg. prochlorperazine as the ethanedisulfonate, 5 mg. sodium biphosphate, 12 mg. sodium tartrate, 0.9 mg. of sodium saccharin and 0.75% benzyl alcohol as preservative.

Suppositories, 2½ mg. (for young children), 5 mg. (for older children) and 25 mg. (for adults), in boxes of 6. Each suppository contains: 2½ mg., 5 mg., or 25 mg. of prochlorperazine with glycerin, glyceryl monopalmitate, glyceryl monostearate, hydrogenated cocoanut oil fatty acids, hydrogenated palm kernel oil fatty acids and lecithin.

Syrup, 5 mg./teaspoonful (5 cc.), in 4 fl. oz. bottles. Each 5 cc. contains 5 mg. of prochlorperazine as the ethanedisulfonate.

Concentrate (for hospital use), 10 mg./cc. in 4 fl. oz. bottles, cartons of 12 and 36. Each cc. contains 10 mg. of prochlorperazine as the ethanedisulfonate.

Prescribing information also available in *Compazine® Reference Manual, Physicians' Desk Reference,* or from your SK&F representative or your pharmacist.

Prescribing information adopted January 1961.

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# STELAZINE®

brand of trifluoperazine

# PRESCRIBING INFORMATION

## INDICATIONS

**In general practice and in psychiatry** 'Stelazine' is outstanding among tranquilizers because it relieves anxiety, agitation and tension—without sedation. Nor does it cause euphoria. 'Stelazine' is also effective in relieving anxiety either accompanying or causing somatic conditions. Where anorexia and insomnia are problems, 'Stelazine' usually produces a marked improvement in appetite and sleep patterns.

'Stelazine' provides a fast therapeutic response. On a convenient b.i.d. dosage regimen, many patients who have failed to respond to other agents, or have responded only poorly, are promptly relieved of their symptoms. With symptoms allayed, rapport with the physician is facilitated, and patients are more receptive to counselling or psychotherapy.

**In hospitalized psychiatric patients** 'Stelazine' produces rapid response in many diagnostic categories. These include acute and chronic schizophrenias, manic-depressive psychoses, involutional psychoses, chronic brain syndrome and mental deficiency.

'Stelazine' can combat psychotic symptoms without causing drowsiness. It can quiet hyperactive patients and activate withdrawn patients, and it has a marked beneficial effect on delusions and hallucinations.

'Stelazine' can rapidly terminate acute psychotic episodes. On the admissions service, intensive 'Stelazine' therapy often results in early discharges.

Also noteworthy is the effectiveness of 'Stelazine' in the treatment of hard-core, chronic and refractory schizophrenics. When administered to a group of such patients, it characteristically produces significant improvement in at least 30% to 40% of them.

## ADMINISTRATION AND DOSAGE

Dosage of 'Stelazine' should be adjusted to the needs of the individual.

*Trademark Reg. U.S. Pat. Off.: 'Benadryl' for diphenhydramine hydrochloride, Parke-Davis.

1. Adult Dosage for Use in Everyday Practice

The recommended dosage is 1 mg. or 2 mg. twice daily. In everyday practice, optimal results are usually achieved within this range, so that it is seldom necessary to exceed 4 mg. daily.

Because of the inherent long action of 'Stelazine', patients may be controlled on convenient b.i.d. administration; some patients may be maintained on once-a-day administration.

2. Adult Dosage for Use in Psychiatric Practice

*oral (for office patients and outpatients with anxiety):* The usual starting dosage is 1 mg. or 2 mg. b.i.d. In the treatment of these patients, it is seldom necessary to exceed 4 mg. a day. (Some patients with more severe disturbances, and discharged mental patients, may require higher dosages.) In some patients, maintenance dosage can be reduced to once-a-day administration.

*oral (for patients who are either hospitalized or under adequate supervision):* The usual starting dosage is 2 mg. to 5 mg. b.i.d. (Small or emaciated patients should always be started on the lower dosage.)

The majority of patients will show optimum response on 15 mg. or 20 mg. daily, although a few may require 40 mg. a day or more. It is important to give doses that are high enough for long enough periods of time – especially in chronic patients.

Optimum therapeutic dosage levels should be reached within two or three weeks after the start of therapy. When maximum therapeutic response is achieved, dosage may be reduced gradually to a satisfactory maintenance level.

*intramuscular (for prompt control of severe symptoms):* The usual dosage is 1 mg. to 2 mg. (½-1 cc.) by deep intramuscular injection q4-6h, p.r.n. More than 6 mg. within 24 hours is rarely necessary. As soon as a satisfactory response is observed, oral medication should be substituted at the same dosage level or slightly higher.

Only in very exceptional cases should intramuscular dosage exceed 10 mg. within 24 hours. Since 'Stelazine' has a relatively long duration of action, injections should not be given at intervals of less than 4 hours because of the possibility of an excessive cumulative effect.

'Stelazine' Injection has been exceptionally well tolerated; there is little, if any, pain and irritation at the site of injection.

3. Dosage for Psychotic and Mentally Defective Children

The dosages given below apply to children, ages 6 to 12, who are either hospitalized or under adequate supervision.

*oral:* The starting dosage is 1 mg. administered once a day or b.i.d., depending on the size of the child. Dosage may be increased gradually until symptoms are controlled or until side effects become troublesome. Both the rate and the amount of dosage increases should be carefully adjusted to the size of the child and the severity of the symptoms, and the lowest effective dosage should always be used. Once control is achieved, it is usually possible to reduce dosage to a satisfactory maintenance level.

In most cases, it is not necessary to exceed 15 mg. of 'Stelazine' daily. However, some older children with severe symptoms may require, and be able to tolerate, higher dosages.

*intramuscular:* There has been little experience with the use of 'Stelazine' Injection in children. However, if it is necessary to achieve rapid control of severe symptoms, 1 mg. (½ cc.) of 'Stelazine' may be administered intramuscularly once or twice a day, depending on the size of the child. Once control is achieved, usually after the first day, the oral dosage forms of 'Stelazine' should be substituted for the Injection.

## SIDE EFFECTS

*In the dosage range of 2-4 mg. daily,* side effects from 'Stelazine' are infrequent. When they do occur, they are usually slight and transitory. Mild drowsiness occurs in a small percentage of patients; this usually disappears after a day or two of 'Stelazine' therapy. There are occasional cases of dizziness, mild skin reaction, dry mouth, insomnia and fatigue; rarely, neuromuscular (extrapyramidal) reactions.

*In hospitalized psychiatric patients* receiving daily 'Stelazine' dosages of 10 mg. or more, clinical experience has shown that, when side effects occur, their appearance is usually restricted to the first two or three weeks of therapy. After this initial period, they appear infrequently, even in the course of prolonged therapy. Termination of 'Stelazine' therapy because of side effects is rarely necessary.

Side effects observed include dizziness, muscular weakness, extrapyramidal symptoms, anorexia, rash, lactation and blurred vision. Drowsiness has occurred, but has been transient, usually disappearing in a day or two.

*Neuromuscular (Extrapyramidal) Reactions*

These symptoms are seen in a significant number of hospitalized mental patients receiving 'Stelazine'. They may be characterized by motor restlessness, be of the dystonic type, or they may resemble parkinsonism.

*motor restlessness:* Some patients may experience an initial transient period of stimulation or jitteriness, chiefly characterized by motor restlessness and sometimes insomnia. These patients should be reassured that this effect is temporary and will disappear spontaneously. The dosage of 'Stelazine' should not be increased while these side effects are present.

If this turbulent phase becomes too troublesome, the symptoms can be controlled by a reduction of dosage or the concomitant administration of a barbiturate.

*dystonias:* These symptoms are rare outside of mental hospitals, but they may be observed occasionally in patients who have received 'Stelazine' as a mild tranquilizer.

Symptoms may include: spasm of the neck muscles, sometimes progressing to torticollis; extensor rigidity of back muscles, sometimes progressing to opisthotonos; carpopedal spasm, trismus, swallowing difficulty, oculogyric crisis and protrusion of the tongue.

The onset of the dystonias may be sudden. A primary characteristic of these symptoms is their intermittency. They may last several minutes, disappear and then recur. There is typically no loss of consciousness and definite prodromata are usually present. Initially, these intermittent symptoms occur in a crescendo of intensity. Then as the effect of the drug wears off, the intervals between the occurrence of symptoms become longer, and the intensity of the symptoms subsides.

Despite their similarity to symptoms of serious neurological disorders, these dystonias are usually promptly reversible and need not cause undue alarm. They usually subside gradually within a few hours, and almost always within 24 to 48 hours, after the drug has been temporarily discontinued. If 'Stelazine' therapy is discontinued, it should be reinstituted at a lower dosage.

Treatment is symptomatic and conservative. *In mild cases,* reassurance of the patient is often sufficient therapy. Barbiturates are also useful. *In moderate cases,* barbiturates will usually bring rapid relief. The dosage and route of administration of the barbiturate used should be determined by the intensity of the symptoms and the response of the patient. *In more severe adult cases,* the administration of an anti-parkinsonism agent (see *Physicians' Desk Reference*) produces rapid, often dramatic, reversal of symptoms. Also, intravenous caffeine and sodium benzoate seems to be an effective and rapid antagonist to the dystonias. Depending on the severity of the dystonia, suitable supportive measures such as maintaining a clear airway and adequate hydration should be employed. *In children,* reassurance and barbiturates will usually control symptoms. Dosage and route of administration should be determined according to the intensity of symptoms and response of patient.

Note: It has been reported that injectable administration of 'Benadryl' may also be helpful in controlling dystonias.

*pseudo-parkinsonism:* These symptoms are extremely rare outside of mental hospitals.

Symptoms include: mask-like facies; drooling; tremors; pill-rolling motion; and shuffling gait.

Reassurance and sedation are important components of effective therapy. In the majority of cases these symptoms are readily reversible when an anti-parkinsonism agent is administered concomitantly with 'Stelazine'. Occasionally it is necessary to lower the dosage or to temporarily discontinue the drug. Depending on the severity of symptoms, suitable supportive measures such as maintaining a clear airway and adequate hydration should be employed. If 'Stelazine' therapy is discontinued, it should be reinstituted at a lower dosage.

## CAUTIONS

Clinical experience has demonstrated that 'Stelazine', a phenothiazine derivative, has a wide range of safety and that there is little likelihood of either blood or liver toxicity. The physician should be aware, however, of their possible occurrence.

One of the results of 'Stelazine' therapy may be an increase in mental and physical activity. In some patients, this effect may not be desired. For example, although 'Stelazine' has relieved anxiety and, at the same time, anginal pain in patients with angina pectoris, a few such patients have complained of increased pain while taking 'Stelazine'. Therefore, if 'Stelazine' is used in angina patients, they should be observed carefully and, if an unfavorable response is noted, the drug should be withdrawn.

Hypotension has not been a problem, but nevertheless adequate precautions should be taken when the drug is used in patients with impaired cardiovascular systems.

The antiemetic action of 'Stelazine' may mask signs of overdosage of toxic drugs or may obscure the diagnosis of conditions such as intestinal obstruction and brain tumor.

Although 'Stelazine' has shown very little potentiating activity, caution should be observed when it is used in large doses in conjunction with sedatives or depressants.

## CONTRAINDICATIONS

'Stelazine' is contraindicated in comatose or greatly depressed states due to central nervous system depressants.

## AVAILABLE

**Tablets,** 1 mg. and 2 mg., in bottles of 50, 500 and 5000. (Each tablet contains 1 mg. or 2 mg. of trifluoperazine as the dihydrochloride.)

For psychiatric patients who are hospitalized or under close supervision:

**Tablets,** 5 mg. and 10 mg., in bottles of 50, 1500 and 5000. (Each tablet contains 5 mg. or 10 mg. of trifluoperazine as the dihydrochloride.)

**Multiple-dose Vials,** 10 cc. (2 mg./cc.), in boxes of 1 and 20. (Each cc. contains, in aqueous solution, 2 mg. of trifluoperazine as the dihydrochloride, 4.75 mg. of sodium tartrate, 11.6 mg. of sodium biphosphate, 0.3 mg. of sodium saccharin, and 0.75% of benzyl alcohol as preservative.)

**Concentrate** (for hospital use), 10 mg./cc., in 2 fl. oz. bottles, in cartons of 4 and 12. (Each cc. contains 10 mg. of trifluoperazine as the dihydrochloride.)

Prescribing information adopted July 1961

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# PARNATE®

brand of tranylcypromine

# PRESCRIBING INFORMATION

The physician should be familiar with the material on dosage, side effects and cautions given below before prescribing 'Parnate', and with the principles of monoamine oxidase inhibitor therapy and the side effects of this class of drugs as reported in the literature. Also, the physician should be familiar with the symptomatology of mental depressions and alternative methods of treatment to aid in the careful selection of patients for 'Parnate' therapy.

## INDICATIONS AND LIMITATIONS OF USE

'Parnate' is indicated for the relief of symptoms of mental depression which may include dejected mood, self-depreciation, lowered activity levels, difficulty in making decisions, disturbed eating and sleeping patterns, and variations of these basic symptoms as described in the literature. The therapeutic utility of monoamine oxidase inhibitors is limited specifically to depressive symptoms; these drugs may aggravate some co-existing symptoms such as agitation or anxiety.

In psychiatry, 'Parnate' is indicated in the following diagnostic categories, subject to the limitation stated above: reactive and other psychoneurotic depressions, involutional melancholia, depressive phase of manic-depressive psychosis, psychotic depressive reactions. In the psychiatric treatment of severe endogenous depressions, it is impossible to predict, with presently known data, which patients will respond best to 'Parnate' and which to ECT. 'Parnate' may be indicated in some reactive depressions in which ECT is not indicated. 'Parnate' is not recommended to treat essentially normal responses to temporary situational difficulties.

*Note:* In depressed patients, the possibility of suicide should always be considered and adequate precautions taken. Exclusive reliance on drug therapy to prevent suicidal attempts is unwarranted, as there may be a delay in the onset of therapeutic effect or an increase in anxiety and agitation. Also, of course, some patients fail to respond to drug therapy.

## CLINICAL EXPERIENCE

Extensive clinical trials with 'Parnate' have confirmed its effectiveness and versatility. As always in the evaluation of drugs for psychic disorders, some variation in efficacy has been reported.

These studies provide the following data on the effectiveness and fundamental properties of 'Parnate':

1. In 500 patients on whom complete data are available for statistical analysis, marked or moderate improvement was reported in 77% of the nonpsychotic patients. Marked improvement was reported in 40% and moderate improvement in 27% of the psychotic patients. Some investigators have pointed out that improvement in certain instances, particularly in milder cases, may have been due to spontaneous remission of symptoms.
2. Improvement is seen within 48 hours to three weeks after starting 'Parnate'; the response can be accelerated by using higher than standard initial dosages.
3. 'Parnate' acts primarily as an antidepressant rather than as a euphoriant. Patients feel essentially normal on 'Parnate' therapy.
4. 'Parnate' can facilitate psychotherapy by increasing the patient's willingness to exert mental effort and reducing symptom-centered preoccupations.
5. 'Parnate' appears to prevent relapses in some patients who have been treated initially with ECT.

## DOSAGE

Dosage should be adjusted to the requirements of the individual patient. Dosage increases should be made only in increments of 10 mg. per day and ordinarily at intervals of one to three weeks. Side effects occur more often as dosage is increased.

Reduction from peak to maintenance dosage may be desirable before withdrawal. If withdrawn prematurely, original symptoms will recur. No tendency to produce rebound depressions of greater intensity has been seen with 'Parnate', although this is a theoretical possibility in patients treated at high dosages. Experimental work indicates that inhibition of monoamine

oxidase persists for only a few days after withdrawal. Thus, any side effects due to this inhibition will probably recede rapidly upon withdrawal, which should be a distinct advantage of 'Parnate' therapy when the patient exhibits poor tolerance to antidepressant medication.

Because there is a striking relationship between dosage and speed of response, two dosage schedules are provided:

**A. Standard dosage.** (This schedule will not always produce prompt results, but it will hold the incidence of side effects to a minimum.)

1. Recommended starting dosage is 20 mg. per day – administered 10 mg. b.i.d. (morning and afternoon).
2. Continue this dosage for two to three weeks.
3. If no signs of a response appear, increase dosage to 30 mg. daily—20 mg. upon arising and 10 mg. in the afternoon.
4. Continue this dosage for at least a week.
5. As soon as a satisfactory response is obtained, dosage may usually be reduced to a maintenance level.
6. Some patients will be maintained on 20 mg. per day; many will need only 10 mg. daily.
7. If dosages above 30 mg. daily are desired for use in exceptionally resistant cases, refer to the schedule of intensive dosage.

**B. Intensive dosage (for accelerated response).** (This schedule is for use in hospitalized patients or those under comparable supervision whenever a prompt effect is more desirable than a relative absence of side effects.)

1. Recommended starting dosage is 30 mg. per day. Administer 20 mg. in the morning and 10 mg. in the afternoon.
2. Continue this dosage for one week.
3. If no signs of a response appear, increase dosage gradually at intervals of several days to one week.
4. Dosages above 60 mg. per day are not advisable.
5. As soon as a satisfactory response is obtained, dosage may usually be reduced gradually to a maintenance level.
6. Some patients may be maintained on 20 mg. per day; many will need only 10 mg. daily.

*Note:* When ECT is being administered concurrently, 10 mg. b.i.d. can usually be given during the series, then reduced to 10 mg. daily for maintenance therapy.

## SIDE EFFECTS

**A. At standard dosages.** Side effects in patients treated with standard doses of 'Parnate' are qualitatively the same as seen at higher dosages but are generally less frequent and less severe.

The patient may experience restlessness, overstimulation, or insomnia; may notice some weakness, drowsiness, episodes of dizziness, or dry mouth; or may report nausea, diarrhea, abdominal pain, or constipation. Occasionally, headaches have occurred. Symptoms of postural hypotension have been seen most commonly, but not exclusively, in patients with pre-existent hypertension; blood pressure returns to pretreatment levels rapidly upon discontinuation of the drug. Other side effects which might occur in rare instances are tachycardia, urinary retention, significant anorexia, skin rashes, edema, palpitations, blurred vision, tinnitus, chills, paresthesia, muscle spasm and tremors, impotence, sweating and possibly paradoxical hypertension.

Most of these side effects can usually be relieved by lowering the dosage or by giving suitable concomitant medication.

**B. At intensive treatment dosages.** When 'Parnate' is used for intensive treatment to control symptoms more rapidly, an increase in the incidence and severity of side effects must be anticipated.

At doses above 30 mg. daily, postural hypotension is a major side effect of 'Parnate' therapy. It affects largely the systolic readings and occurs mainly, but not exclusively, in patients with a history of hypertension. Rare instances of syncope have been seen. Dosage increases should be made more gradually in patients showing a tendency toward hypotension at the starting dose. Postural hypotension can be relieved by having the patient lie down until blood pressure returns to normal.

Other side effects which may occur are listed above under *standard dosages*. Headaches have occasionally been severe and incapacitating. Overstimulated behavior, which may include increased anxiety, agitation and manic symptoms, can be evidence of either a side effect or an excessive therapeutic action; if this occurs, reduce dosage or administer a phenothiazine tranquilizer.

## CAUTIONS

Extensive clinical and laboratory work has shown that there is little likelihood of blood or liver toxicity. Since 'Parnate' is a non-hydrazine compound, it should prove to be exempt from the toxic effects on the liver thought to be due to the hydrazine moiety of some other drugs. However, severe toxic reactions have occurred with some monoamine oxidase inhibitors. Pending further clinical experience, 'Parnate' should probably not be used in patients with a history of liver disease or in those with abnormal liver function tests. Drug-induced jaundice is often difficult to differentiate from other jaundice. However, there has been sufficient clinical experience with 'Parnate' to demonstrate that, if it has any potentiality for producing jaundice, the reaction must be rare. Also, the usual precautions should be observed in patients with impaired renal function since there is a possibility of accumulative effects in such patients.

Although 'Parnate' has been used in combination with various drugs (particularly Stelazine®, brand of trifluoperazine), some monoamine oxidase inhibitors have been reported to have marked potentiating effects on certain drugs, e.g., sympathomimetics, central nervous system depressants, hypotensive agents and alcohol. Therefore, the physician should bear in mind the possibility of a lowered margin of safety when 'Parnate' is combined with potent drugs and should adjust dosage carefully. 'Parnate' should not be used in combination with imipramine. (The reaction of a patient who attempted suicide with a deliberate overdosage of 'Parnate' and imipramine was more severe than would have been predicted from the properties of either drug.)

## CASES REQUIRING SPECIAL CONSIDERATION

Administer with caution to patients with recent myocardial infarction or coronary artery disease with angina of effort. Increased physical activity and, more rarely, hypotension have been reported. The pharmacologic properties of 'Parnate' suggest that it may have a capacity to suppress anginal pain that would otherwise serve as a warning sign of myocardial ischemia. When 'Parnate', like any agent which lowers blood pressure, is withdrawn from patients who tend to be hypertensive, blood pressure may again rise to undesirable levels.

When 'Parnate' is combined with a phenothiazine derivative or other compound known to affect blood pressure, elderly patients and those with cardiovascular inadequacies should be observed more closely because of the possibility of additive hypotensive effects.

In patients being transferred to 'Parnate' from another monoamine oxidase inhibitor or from imipramine, allow a medication-free interval of one week, then initiate 'Parnate' using half the normal dosage for at least the first week of therapy. Similarly, a few days should elapse between the discontinuance of 'Parnate' and the administration of another monoamine oxidase inhibitor or of imipramine.

Because the influence of 'Parnate' on the convulsive threshold is variable in animal experiments, suitable precautions should be taken if epileptic patients are treated.

## AVAILABLE

**Tablets,** 10 mg.; in bottles of 50 and 1500. (Each tablet contains 10 mg. of tranylcypromine, as the sulfate.)

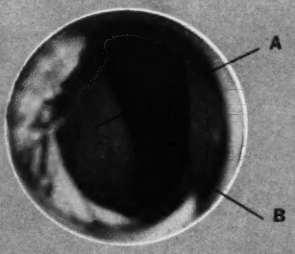
Prescribing information adopted Feb. 1961.

# 24-hour relief of running nose, sneezing and nasal stuffiness of "colds" with

# ONE ORNADE® SPANSULE® q12h

brand of sustained release capsules

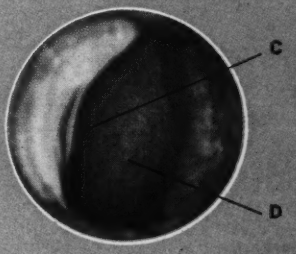
**the unique oral nasal decongestant with a special drying agent**




**BEFORE TAKING 'ORNADE'**

**A—Note enlargement of turbinate, partially closing airway.**

**B—Septum is in deep shadow and is only partly visible since little light penetrates past swollen turbinate into nostril.**




**12 HOURS AFTER TAKING 'ORNADE'**

**C—Turbinate has shrunk to normal. Patency of airway, established by 2nd hour, is maintained into 12th hour.**

**D—A larger area of septum is visible and is clearly seen as more light penetrates to rear of nostril.**

PRESCRIBING INFORMATION

The comprehensive formula of 'Ornade' *Spansule* capsules contains a special drying agent, isopropamide iodide, in addition to a decongestant and an antihistamine. Isopropamide iodide acts to reduce excessive weeping and nasal and paranasal secretions. The decongestant, phenylpropanolamine, reduces vascular engorgement and often permits blocked sinus cavities to drain. The antihistamine, 'Teldrin', reduces sneezing, rhinorrhea and itching of the eyes. Acting together, additively, these three agents combine to provide outstanding relief from upper respiratory distress.

FORMULA: Each 'Ornade' *Spansule* sustained release capsule contains 8 mg. of Teldrin® (brand of chlorpheniramine maleate) and 50 mg. of phenylpropanolamine hydrochloride, so prepared that a therapeutic dose is released promptly and the remaining medication, released gradually and without interruption, sustains the effect for 10 to 12 hours; and 2.5 mg. of isopropamide, as the iodide. Because isopropamide iodide is inherently long-acting, it has not been necessary to put it into sustained release form; therefore, the entire dose of isopropamide iodide is released upon ingestion.

INDICATIONS: 'Ornade' *Spansule* capsules are recommended for prompt and prolonged relief from respiratory tract congestion and hypersecretion associated with: the common cold, acute, subacute and chronic sinusitis, influenza, vasomotor rhinitis, postnasal drip, allergic rhinitis: hay fever, "rose fever," etc.

DOSAGE (adults and children over 6): For all-day, all-night relief, one 'Ornade' *Spansule* capsule q12h. When taken at bedtime, 'Ornade' keeps patients symptom-free throughout the night and usually enables them to wake up in the morning uncongested and with airways free.

SIDE EFFECTS: Drowsiness, "nervousness," or insomnia may occur on rare occasions, but are usually mild and transitory.

CAUTIONS AND CONTRAINDICATIONS: Use with caution in the presence of severe hypertension. 'Ornade' should not be used in patients with glaucoma or prostatic hypertrophy. NOTE: The iodine in isopropamide iodide may alter PBI test results and will suppress $I^{131}$ uptake.

SUPPLIED: In bottles of 30 capsules.

Prescribing information adopted January, 1961.

SK&F *Smith Kline & French Laboratories*